

Table S1. LDLR, APOB and PCSK9 variants identified in the Romanian FH cohort and not reported previously in this population.
REFERENCE SEQUENCE: NM_000527.5 for LDLR, NM_000384.3 for APOB, NM_174936.3 for PCSK9

ID	GENE	EXON /INTRON	DOMAIN	cDNA change	Protein change	dbSNP ID	ClinVar assertion	LOVD/HGMD annotation and assertion	Sanger confirmation	CV events
H7	LDLR LDLR	10 11	EGF precursor LDLR class B4	c.1413A>G c.1617C>T	p.(Arg471=) p.(Pro539=)	rs5930 He rs5929 He	Benign Benign	Benign Benign	YES	YES Stroke
H8	LDLR LDLR LDLR	11 12 13	LDLR class B4 LDLR class B5 LDLR class B6	c.1617C>T c.1773C>T c.1959T>C	p.(Pro539=) p.(Asn591=) p.(Val653=)	rs5929 rs688 Ho rs5925 Ho	Benign Likely benign Likely benign	Benign Benign Benign	YES	YES Stroke
H10	LDLR LDLR	7 7i	NA Intron	c.1060+7= c.1060+10G>A	NA NA	rs2738442 rs12710260 Ho	Conflicting interpretations Conflicting interpretations	No referenced Conflicting interpretations	YES	NO
H14	LDLR LDLR	12 13	LDLR class B5 LDLR class B6	c.1773C>T c.1959T>C	p.(Asn591=) p.(Val653=)	rs5929 rs5925 He	Benign Likely benign	Benign Benign	YES	NO
H15	LDLR LDLR	7 7i	NA Intron	c.1060+7= c.1060+10G>A	NA NA	rs2738442 rs12710260 Ho	Conflicting interpretations Conflicting interpretations	No referenced Conflicting interpretations	YES	NO
H16	LDLR LDLR	12 13	LDLR class B5 LDLR class B6	c.1773C>T c.1959T>C	p.(Asn591=) p.(Val653=)	rs5929 rs5925 He	Benign Likely benign	Benign Benign	YES	NO
H18	LDLR LDLR LDLR LDLR LDLR LDLR LDLR	2 7 7i 10 12 13 15	ligand-binding NA Intron LDLR class B2 LDLR class B5 LDLR class B6 clustered O-linked oligosaccharides	c.81C>G c.1060+7= c.1060+10G>A c.1413A>G c.1773C>T c.1959T>C c.2232A>G	p.(Cys27Trp) NA NA p.(Arg471=) p.(Asn591=) p.(Val653=) p.(Arg744=)	NA rs2738442 rs12710260 Ho rs5930 rs688 Ho rs5925 Ho rs5927 Ho	Likely pathogenic Conflicting interpretations Benign Likely benign Benign Likely benign Benign	Probably pathogenic No referenced Conflicting interpretations Benign Benign Benign Benign	YES	YES Stroke
H19	LDLR LDLR LDLR LDLR PCSK9	7 10 11 12 7	NA LDLR class B2 LDLR class B4 LDLR class B5 NA	c.1060+7= c.1413A>G c.1618G>A c.1773C>T c.1026A>G	NA p.(Arg471=) p.(Ala540Thr) p.(Asn591=) p.(Gln342=)	rs2738442 rs5930 NA rs688 Ho rs509504 Ho	Conflicting interpretations Benign Pathogenic Likely benign Conflicting interpretations	No referenced Benign Likely pathogenic Benign No referenced	YES	YES ACS
H24	LDLR LDLR	7 15	NA clustered O-linked oligosaccharides	c.1060+7= c.2232A>G	NA p.(Arg744=)	rs2738442 rs5927 Ho	Conflicting interpretations Benign	No referenced Benign	YES	YES PAD
H25	LDLR	15	clustered O-linked	c.2232A>G	p.(Arg744=)	rs5927 Ho	Benign	Benign	YES	NO

			oligosaccharides							
H26	PCSK9 APOB	7 26	NA NA	c.1026A>G c.10740C>T	p.(Gln342=) p.(Asn3580=)	rs509504 Ho rs150312765	Conflicting interpretations Benign	No referenced No referenced	YES YES	PAD PAD
H32	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced	YES	YES
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		Stroke
	LDLR	12	LDLR class B5	c.1773C>T	p.(Asn591=)	rs688 He	Likely benign	Benign		
	LDLR	13	LDLR class B6	c.1959T>C	p.(Val653=)	rs5925 He	Likely benign	Benign		
	LDLR	15	clustered O-linked oligosaccharides	c.2232A>G	p.(Arg744=)	rs5927 He	Benign	Benign		
	PCSK9	7	NA	c.1026A>G	p.(Gln342=)	rs509504 Ho	Conflicting interpretations	No referenced		
H40	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced	YES	YES
	LDLR	7i	Intron	c.1060+10G>A	NA	rs12710260 He	Conflicting interpretations	Conflicting interpretations		ACS
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	12	LDLR class B5	c.1773C>T	p.(Asn591=)	rs688 He	Likely benign	Benign		
	LDLR	13	LDLR class B6	c.1959T>C	p.(Val653=)	rs5925 He	Likely benign	Benign		
	PCSK9	7	NA	c.1026A>G	p.(Gln342=)	rs509504 Ho	Conflicting interpretations	No referenced		
H41	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced	YES	YES
	LDLR	7i	NA	c.1060+10G>A	NA	rs12710260	Conflicting interpretations	Conflicting interpretations		Stroke
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	12	LDLR class B5	c.1773C>T	p.(Asn591=)	rs688 He	Likely benign	Benign		
	LDLR	13	LDLR class B6	c.1959T>C	p.(Val653=)	rs5925 He	Likely benign	Benign		
	LDLR	15	clustered O-linked oligosaccharides	c.2232A>G	p.(Arg744=)	rs5927 He	Benign	Benign		
	LDLR	12i_15i	A750GfsX29; FH Bologna-2	c.(1845+1_1846-1)_(2311+1_2312-1)dup	exon 13-15		Pathogenic	Pathogenic		
H44	LDLR	2	LDLR class A1	c.81C>T	p.(Cys27=)	rs2228671	Benign	Benign	YES	YES
	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced		ACS
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	11	LDLR class B4	c.1617C>T	p.(Pro539=)	rs5929 Ho	Benign	Benign		
	LDLR	15	clustered O-linked oligosaccharides	c.2232A>G	p.(Arg744=)	rs5927 Ho	Benign	Benign		
	LDLR	11	LDLR class B4	c.1618G>A	p.(Ala540Thr)	NA	Pathogenic	Likely pathogenic		
H46	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced	YES	YES
	LDLR	7i	Intron	c.1060+10G>A	NA	rs12710260 He	Conflicting interpretations	Conflicting interpretations		ACS
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	11	LDLR class B4	c.1618G>A	p.(Ala540Thr)	NA	Pathogenic	Likely pathogenic		

	LDLR LDLR LDLR	12 13 15	LDLR class B5 LDLR class B6 clustered O-linked oligosaccharides	c.1773C>T c.1959T>C c.2232A>G	p.(Asn591=) p.(Val653=) p.(Arg744=)	rs688 He rs5925 He rs5927 He	Likely benign Likely benign Benign	Benign Benign Benign		
H51	LDLR LDLR LDLR LDLR LDLR APOB	3 7 10 13 15 26	NA NA LDLR class B2 LDLR class B6 clustered O-linked oligosaccharides NA	c.211G>A c.1060+7= c.1413A>G c.1959T>C c.2232A>G c.10740C>T	p.(Gly71Arg) NA p.(Arg471=) p.(Val653=) p.(Arg744=) p.(Asn3580=)	rs766903209 rs2738442 rs5930 rs5925 He rs5927 He rs150312765	Conflicting interpretations Conflicting interpretations Benign Likely benign Benign Benign	No referenced No referenced Benign Benign Benign No referenced	YES YES YES YES YES YES	YES ACS YES YES YES YES
H52	LDLR LDLR LDLR LDLR LDLR LDLR PCSK9 APOB	2 7 10 12 13 15 7 26	ligand-binding NA LDLR class B2 LDLR class B5 LDLR class B6 clustered O-linked oligosaccharides NA NA	c.81 C>G c.1060+7= c.1413A>G c.1773C>T c.1959T>C c.2232A>G c.1026A>G c.10740C>T	p.(Cys27Trp) NA p.(Arg471=) p.(Asn591=) p.(Val653=) p.(Arg744=) p.(Gln342=) p.(Asn3580=)	NA rs2738442 rs5930 rs688 He rs5925 He rs5927 He rs509504 Ho rs150312765	Likely pathogenic Conflicting interpretations Benign Likely benign Likely benign Benign Conflicting interpretations Benign	Likely pathogenic No referenced Benign Benign Benign Benign No referenced No referenced	YES YES YES YES YES YES YES YES	YES PAD YES YES YES YES YES YES
H53	LDLR LDLR LDLR LDLR PCSK9	7 10 11 15 7	NA LDLR class B2 LDLR class B4 clustered O-linked oligosaccharides NA	c.1060+7= c.1413A>G c.1618G>A c.2232A>G c.1026A>G	NA p.(Arg471=) p.(Ala540Thr) p.(Arg744=) p.(Gln342=)	rs2738442 rs5930 NA rs5927 He rs509504 Ho	Conflicting interpretations Benign Pathogenic Benign Conflicting interpretations	No referenced Benign Pathogenic Benign No referenced	YES YES YES YES YES	YES ACS YES YES YES
H54	LDLR LDLR LDLR LDLR	4 7 10 15	LDLR class A4 NA LDLR class B2 clustered O-linked oligosaccharides	c.502G>A c.1060+7= c.1413A>G c.2232A>G	p.(Asp168Asn) NA p.(Arg471=) p.(Arg744=)	rs200727689 rs2738442 rs5930 rs5927 He	Pathogenic Conflicting interpretations Benign Benign	Likely pathogenic No referenced Benign Benign	YES YES YES YES	YES Stroke YES YES
H55	LDLR LDLR LDLR LDLR LDLR	2 7 7i 10 15	LDLR class A1 NA Intron LDLR class B2 clustered O-linked	c.81C>T c.1060+7= c.1060+10G>A c.1413A>G c.2232A>G	p.(Cys27=) NA NA p.(Arg471=) p.(Arg744=)	rs2228671 rs2738442 rs12710260 He rs5930 rs5927 Ho	Benign Conflicting interpretations Conflicting interpretations Benign Benign	Benign No referenced Conflicting interpretations Benign Benign	YES YES YES YES YES	NO NO NO NO NO

			oligosaccharides							
H56	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced	YES	NO
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	12	LDLR class B5	c.1773C>T	p.(Asn591=)	rs688 He	Likely benign	Benign		
	LDLR	13	LDLR class B6	c.1959T>C	p.(Val653=)	rs5925 He	Likely benign	Benign		
	LDLR	15	clustered O-linked oligosaccharides	c.2232A>G	p.(Arg744=)	rs5927 Ho	Benign	Benign		
H57	LDLR	2	LDLR class A1	c.81C>T	p.(Cys27=)	rs2228671	Benign	Benign	YES	YES
	LDLR	7	NA	c.1060+7=	NA	rs2738442	Conflicting interpretations	No referenced		PAD
	LDLR	7i	Intron	c.1060+10G>A	NA	rs12710260	Conflicting interpretations	Conflicting interpretations		
	LDLR	10	LDLR class B2	c.1413A>G	p.(Arg471=)	rs5930	Benign	Benign		
	LDLR	12	LDLR class B5	c.1773C>T	p.(Asn591=)	rs688 He	Likely benign	Benign		
	LDLR	13	LDLR class B6	c.1959T>C	p.(Val653=)	rs5925 He	Likely benign	Benign		
	LDLR	15	clustered O-linked oligosaccharides	c.2232A>G	p.(Arg744=)	rs5927 Ho	Benign	Benign		

*Words written in red signify pathogenic mutations