

# WHOLE EXOME SEQUENCING AND 12-SNP LDL POLYGENIC SCORE IN SOUTH INDIAN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Supplementary table 1: Details of VUS

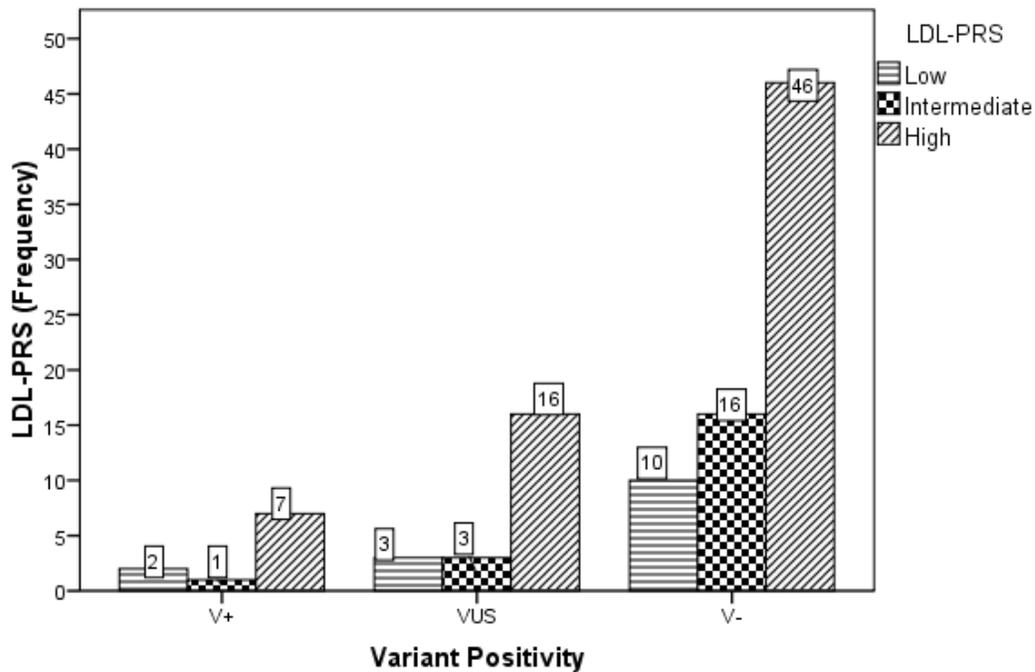
	GENE	LOCATION/ VARIANT TYPE	VARIANT (Amino acid change)	ClinVAR ID	MAF(Gnom AD)	ACMG classification	LDL - PRS/ 	POSITIVE INSILICO PREDICTION TOOLS
V1	<b>LDLR</b>	Intron 10	c.1586+5G>A (5' splice site) g.11113767G>A	251909 (conflicting evidence)	-	PM3	1.025	
V2	<b>LDLR</b>	Intron10	c.1586+5G>A (5' splice site) g.11113767G>A	251909 (conflicting evidence)	-	PM3	1.005	
V3	<b>LDLR</b>	Intron 10	c.1586+5G>A (5' splice site) g.11113767G>A	251909 (conflicting evidence)	-	PM3	1.22	
V4	<b>LDLR</b>	Exon 4/ missense	c.323C>A (p.Thr108Lys) g.11105229C>A	841986	-	PM1, PM2	0.962	Polyphen 2/ SIFT/mutation Taster 2
V5	<b>LDLR</b>	Exon6 Missense	c.938G>C (p.Cys313Ser) g.11107512G>C	-	-	PM1, PM2, PP3,	-	Polyphen 2/ SIFT/LRT/
V6	<b>LDLR</b>	Exon7 missense	c.1057G>A (p.Glu353Lys) g.11110768G>A	161275	0.005%	PM1	-	LRT
V7	<b>LDLR</b>	Exon 13 missense	c.1697G>A (p.Arg566Gln) g.11123264G>A	-	0.07%	PM2, BP4	0.949	Mutation Taster 2
V8	<b>LDLR</b>	Exon14/ missense	c.2093G>C (p.Cys698Ser) g.11120475G>C	1512785	-	PM1, PM2, PM5, PP3	1.004	SIFT/ LRT/ Polyphen 2/ Mutation Taster
V9	<b>LDLR</b>	Exon 14/ missense	c.2093G>C (p.Cys698Ser) g.11120475G>C	1512785	-	PM1, PM2, PM5, PP3	0.849	SIFT/ LRT/ Polyphen 2/ Mutation Taster
V1 0	<b>LDLR</b>	Exon14 Missense	c.2093G>C (p.Cys698Ser) g.11120475G>C	1512785	-	PM1, PM2, PM5, PP3	0.946	SIFT/ LRT/ Polyphen 2/ Mutation Taster
V1 1	<b>PCSK9</b>	Exon 10/ missense	c.1540G>A (p.Ala514Thr) g.55059522G>A	919133	0.0007%	PP3	1.017	SIFT/ LRT/ Polyphen 2
V1 2	<b>APOB</b>	Exon18 missense	c.2702T>G (p.Met901Arg) g.21022945A>C	2565840	-	PM2, BP1	1.029	Polyphen 2/ SIFT

V1 3	<b>APOB</b>	Exon23/ Missense	c.3671G>A (p.Arg1224Gln) g.21015098C>T	630321	0.002%	PM2	0.643	Polyphen 2/ SIFT/LRT/ Mutation Taster 2
V1 4	<b>APOB</b>	Exon25 Missense	c.4072C>G (p.Leu1358Val) g.21013304G>C	630312	-	PM2, BP4	0.988	Polyphen 2
V1 5	<b>APOB</b>	Exon 26 Missense	c.10700C>T (p.Thr3567Met) g.21006168G>A	440520	0.01%	PM2, BP4, BP1	0.53	Mutation Taster 2
V1 6	<b>APOB</b>	Exon26/ Missense	c.11656 C>T (p.Arg3886Cys) g.21005212G>A	2926008	0.001%	PM2	0.836	Polyphen2
V 17	<b>APOE</b>	Exon4 missense	c.873G>C (p.Gln291His) g.44909169G>C	-	-	PM2, BP4	0.996	NA
V 18	<b>ABCG8</b>	Exon9 missense	c.1226A>C (p.Asn409Thr) g.43873801A>C	-	-	PM2, PP3	0.897	Polyphen 2/ SIFT/LRT/
V 19	<b>ABCG5</b>	Exon3/ Missense	c.281C >G (p.Thr94Arg) g.43832068G>C	336053	0.0006%	PM2, PP3	0.977	Polyphen2/ SIFT/LRT/ Mutation taster2
V 20	<b>ABCG5</b>	Intron11	c.1650-2A>T g.43814591T>A	-	-	PVS1, PM2	0.87	Mutation Taster2
V 21	<b>SREBF2</b>	Exon 10 missense	c.1846G>T (p.Ala616Ser) 41880800G>T	3169918	-	PM2, BP4	1.21	Polyphen 2, LRT
V 22	<b>SREBF2</b>	Exon19 Frameshift	c.3353_3359del (p. Asp1118AlafsTer9) g.41905587_419055 93del	-	-	PM2, PP3		---
V 23	<b>PPP1R17</b>	Exon3/ missense	c.169G>A (p.Glu57Lys) g.31695555G>A	-	-	PM2	0.775	SIFT/LRT/Mutati on Taster 2

V 24	<b>PPP1R17</b>	CNV	chr7g (31687307_31687214) (31708456_31707203) dup	-	-		1.1	
V 25	<b>ABCG8</b>	Exon1 Start loss variation	c.2T>C (p.Met1) g.43839055T>C	1677567	0.001%	PVS1, PM2, PP5	0.698	SIFT/Mutation Taster 2
	<b>LDLR</b>	Exon7 missense	c.1057G>A (p.Glu353Lys) g.11110768G>A	161275	0.005%	PM1, PP3, BS2		LRT/ Mutation Taster 2
V2 6	<b>LDLR</b>	Exon 10 missense	c.1567G>C (p.Val523Leu) g.11113743G>C	993226 (conflicting evidence)	0.0007%	PM1, PM2, PM5, PP3		Polyphen 2/ SIFT/LRT/
	<b>LPL</b>	Exon6 missense	c.997C>T (p. Arg333Cys) g.19956062C>T	-	0.002%	PM1, PM2, PM5, PP2, PP3		Polyphen 2/ SIFT/LRT/

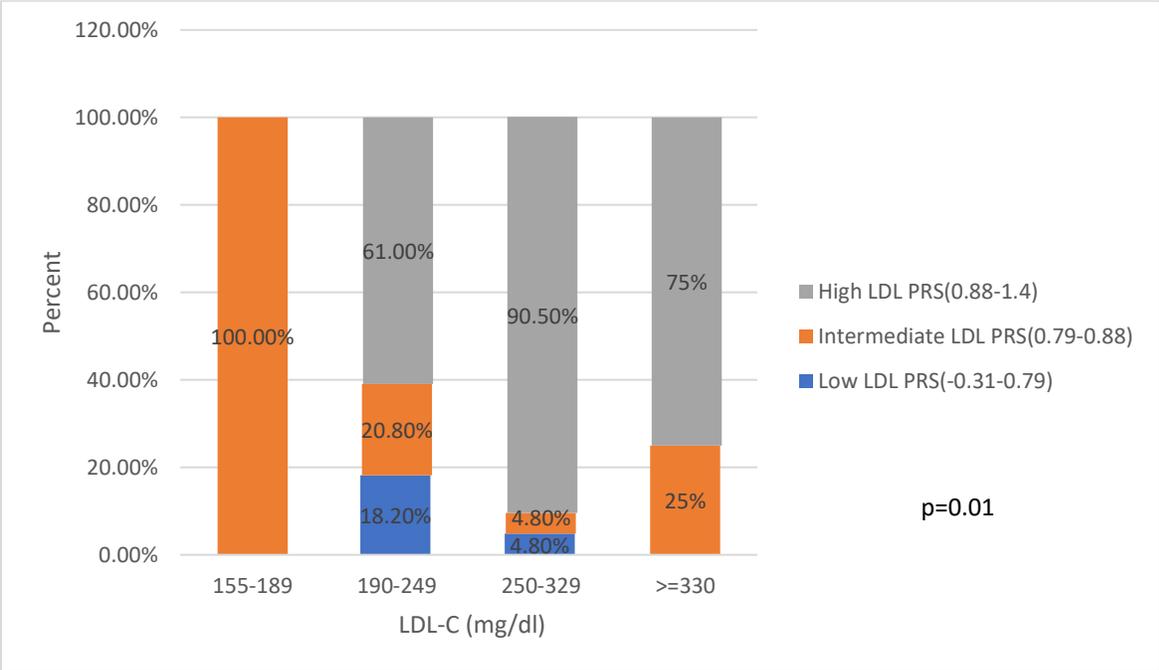
LDLR: Low-density lipoprotein receptor, Apo B: Apolipoprotein B, Apo E: Apolipoprotein E, ABCG5: ATP-binding cassette sub-family G member 5, ABCG8: ATP-binding cassette sub-family G member 8, PPP1R17: Protein phosphatase 1 regulatory subunit 17, SREBF2: Sterol regulatory element-binding protein 2, LPL: Lipoprotein lipase, VUS: Variant of unknown significance, ACMG: American college of Medical Genetics and Genomics, MAF: Minor allele frequency

Supplementary Figure 1: Distribution of LDL-PRS among variants



VUS: variant of unknown significance, PRS: polygenic score

Supplementary figure 2: Correlation between LDL-C and LDL-PRS



PRS: polygenic score