

Supplemental Table 1. ACMG/AMP classification and variant class of the control set variants.

Variant	ClinVar ID	Functional study results ^a		Class of <i>LDLR</i> variant (Cytometry results)	ACMG Classification
		Expression	Activity		
c.1A>T, (p.Met1Leu)	250968	<10%/<10%	<10%/<10%	Class I—Null (16)	Likely pathogenic
c.76A>T, (p.Arg26*)	251006	<10%/<10%	<10%/<10%	Class I – Null (NA)	Pathogenic
c.81C>T, (p.Cys27Cys)	251010	101%/100%	105%/85%	Normal (NA)	Benign
c.261G>A, (p.Trp87*)	251100	<10%/<10%	<10%/<10%	Class I—Null (17)	Pathogenic
c.326G>T, (p.Cys109Phe)	251157	105%/104%	31%/42%	Class III—Binding (19)	Pathogenic
c.427T>C, (p.Cys143Arg)	251219	95%/98%	31%/30%	Class III—Binding (19)	Pathogenic
c.551G>A, p.(Cys184Tyr)	3739	112%/107%	44%/46%	Class III—Binding (18)	Likely pathogenic
c.618_638del, (p.Gly207_Ser213del)	265899	98%/102%	24%/34%	Class III—Binding (18)	Pathogenic
c.661G>T, (p.Asp221Tyr)	251356	101%/108%	27%/45%	Class III—Binding (18)	Pathogenic
c.799G>A, (p.Glu267Lys)	251459	97%/111%	66%/60%	Class III—Binding (19)	Likely pathogenic
c.1054T>A, (p.Cys352Ser)	251617	104%/97%	57%/53%	Class III—Binding (19)	Pathogenic
c.1171G>A, (Ala391Thr)	183138	103%/109%	105%/100%	Normal (NA)	Benign
c.1246C>T, (p.Arg416Trp)	183110	71%/81%	89%/119%	Class V—Recycling (17)	Pathogenic
c.1352T>C, (p.Ile451Thr)	251801	<10%/<10%	<10%/<10%	Class I—Null (19)	Pathogenic
c.1361C>A, (p.Thr454Asn)	251812	80%/85%	86%/89%	Class V—Recycling (17)	Likely pathogenic
c.1413A>G, (p.Arg471Arg)	200916	101%/110%	109%/112%	Normal (NA)	Benign
c.1455C>G, (p.His485Gln)	251851	63%/73%	71%/90%	Class IIb—Expression (19)	Likely pathogenic
c.1474 G>A, p.(Asp492Asn)	161285	69%/80%	73%/73%	Class V—Recycling (19)	Likely pathogenic
c.1499T>C, p.(Val500Ala)	265903	40%/53%	82%/65%	Class IIb—Expression (19)	Likely pathogenic

c.1775G>A, (p.Gly592Glu)	161271	57%/65%	84%/78%	Class V—Recycling (18)	Pathogenic
c.1802A>T, (p.Asp601Val)	252040	<10%/<10%	<10%/<10%	Class I—Null (18)	Pathogenic
c.1840T>A, (p.Phe614Ile)	252061	67%/71%	95%/100%	Class IIb—Expression (19)	Likely pathogenic
c.1876G>A, (p.Glu626Lys)	183127	103%/109%	67%/76%	Class IV—Internalization (19)	Pathogenic
c.1966C>A, (p.His656Asn)	252136	101%/97%	104%/100%	Normal (18)	VUS
c.2177C>T, (p.Thr726Ile)	36461	107%/111%	103%/96%	Normal (NA)	Benign
c.2291T>C, (p.Ile764Thr)	252265	108%/105%	107%/106%	Normal (18)	Likely benign
c.2475C>A, (p.Asn825Lys)	252341	100%/115%	80%/71%	Class IV—Internalization (17)	Likely pathogenic

^aPercentages for the 24-well and 96-well assays, on the left and right, respectively. Percentages in bold represent values below the 70% cutoff, and thus affecting LDLR function. NA = not available.