

Variant: *NM_000527.5(LDLR):c.1837G>A (p.Val613Ile)*

Version: 1.0

CA023595 [↗](#)

161288 (ClinVar) [↗](#)

Gene: LDLR ([HGNC:3949](#))

Condition: hypercholesterolemia, familial ([MONDO:0007750](#))

Inheritance Mode: Semidominant inheritance

UUID: 9ea4b7fb-e7b9-43aa-b887-aaedf6ae8270

Approved on: 2025/3/28

Published on: 2025/6/30

HGVS expressions

NM_000527.5(LDLR):c.1837G>A (p.Val613Ile)

NM_000527.5:c.1837G>A

NC_000019.10:g.11116990G>A

CM000681.2:g.11116990G>A

NC_000019.9:g.11227666G>A

CM000681.1:g.11227666G>A

NC_000019.8:g.11088666G>A

NG_009060.1:g.32610G>A

ENST00000252444.10:c.2095G>A

ENST00000559340.2:c.1705+778G>A

ENST00000560467.2:c.1717G>A

ENST00000558518.6:c.1837G>A

ENST00000252444.9:c.2091G>A

ENST00000455727.6:c.1333G>A

ENST00000535915.5:c.1714G>A

ENST00000545707.5:c.1456G>A

ENST00000557933.5:c.1837G>A

ENST00000558013.5:c.1837G>A

ENST00000558518.5:c.1837G>A

ENST00000559340.1:c.426+778G>A

NM_000527.4:c.1837G>A

NM_001195798.1:c.1837G>A

NM_001195799.1:c.1714G>A

NM_001195800.1:c.1333G>A

NM_001195803.1:c.1456G>A

NM_001195798.2:c.1837G>A

NM_001195799.2:c.1714G>A

NM_001195800.2:c.1333G>A

NM_001195803.2:c.1456G>A

Uncertain Significance

Met criteria codes **3**

PP4

PM2

PS4_Supporting

Not Met criteria codes **18**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

BA1BP4BP3BP2BS1BS4BS3BS2PP1PP3PM6PM1PM3PM5PM4PS1PS2PS3

Evidence Links 0

[Criteria Specification: ClinGen Familial Hypercholesterolemia Expert Panel Specifications to the ACMG/AMP Variant Classification Guidelines Version 1.2](#)[PDF](#)[Criteria Specification Approval History](#)[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1837G>A (p.Val613Ile) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PS4_Supporting and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 28 March 2025. The supporting evidence is as follows: PM2: PopMax MAF = 0.00005340 (0.005%) in African/African American exomes+genomes (gnomAD v4.1.0). PS4_Supporting, PP4: Variant meets PM2 and is identified in 2 unrelated index cases meeting FH criteria (1 case in PMID 19837725 (Whittall et al., 2010), UK; 1 case in PMID 16250003 (Fouchier et al., 2005), Netherlands).

Met criteria codes

PP4			Variant meets PM2 and is identified in 2 unrelated index cases who fulfill clinical criteria for FH from previous studies (see PS4 for details), after alternative causes of high cholesterol were excluded. So, PP4 is met.
PM2			PopMax MAF = 0.00005340 (0.005%) in African/African American exomes+genomes (gnomAD v4.1.0). So, PM2 is met.
PS4_Supporting			Variant meets PM2 and is identified in 2 index cases (1 case with Simon Broome criteria of possible/definite FH in PMID 19837725 (Whittall et al., 2010); 1 case with FH based on Defesche in PMID: 16250003 (Fouchier et al., 2005), Netherlands). So, PS4_Supporting is met.

Not Met criteria codes

BA1			FAF= 0.00001663 in African/African American exomes+genomes (gnomAD v4.1.0).
BP4			REVEL= 0.564. It is above 0.5.
BP3			No in-frame deletions/insertions.
BP2			No data available.
BS1			FAF= 0.00001663 in African/African American exomes+genomes (gnomAD v4.1.0).
BS4			No data available.

BS3			No data available.
BS2			No data available.
PP1			No data available.
PP3			REVEL= 0.564. Functional data on splicing not available. A) variant not on limits. B) variant is exonic and at least 50bp downstream from the canonical acceptor site, but it does not create GT. C) there is no GT nearby. Variant is not predicted to alter splicing.
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			Not on exon 4. Not a cysteine residue.
PM3			No data available.
PM5			The variant is the only variant found in this codon.
PM4			No in-frame deletions/insertions.
PS1			The variant is the only variant found in this codon.
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No data available.

Curation History 		
Showing 1 to 1 of 1 rows		

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

[ClinGen Terms of Use.](#)

[⌕ Powered by BCM's Genboree.](#)