

Variant: NM_000527.5(LDLR):c.48C>A (p.Leu16=)

Version: 1.0

CA085712 [↗](#)

250983 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 18e5ecf5-6d86-4789-b174-8536432b1d44

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HGVS expressions

NM_000527.5:c.48C>A

NM_000527.5(LDLR):c.48C>A (p.Leu16=)

NC_000019.10:g.11089596C>A

CM000681.2:g.11089596C>A

NC_000019.9:g.11200272C>A

CM000681.1:g.11200272C>A

NC_000019.8:g.11061272C>A

NG_009060.1:g.5216C>A

ENST00000559340.2:c.48C>A

ENST00000560467.2:c.48C>A

ENST00000558518.6:c.48C>A

ENST00000455727.6:c.48C>A

ENST00000535915.5:c.48C>A

ENST00000545707.5:c.48C>A

ENST00000557933.5:c.48C>A

ENST00000557958.1:n.134C>A

ENST00000558013.5:c.48C>A

ENST00000558518.5:c.48C>A

ENST00000560502.5:n.134C>A

NM_000527.4:c.48C>A

NM_001195798.1:c.48C>A

NM_001195799.1:c.48C>A

NM_001195800.1:c.48C>A

NM_001195803.1:c.48C>A

NM_001195798.2:c.48C>A

NM_001195799.2:c.48C>A

NM_001195800.2:c.48C>A

NM_001195803.2:c.48C>A

NR_163945.1:n.64G>T

Likely Benign

Met criteria codes **4**

BP4 BP7 PP4 PM2

Evidence Links **0**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5 (LDLR):c.48C>A (p.Leu16=) variant is classified as Likely Benign for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PP4, BP4 and BP7 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 7 November 2023. The supporting evidence is as follows: PM2: PopMax MAF=0.00006 in Latino population in gnomAD (gnomAD v2.1.1). PP4: Variant meets PM2 and is identified in 1 index case with possible FH by Simon Broome criteria, after alternative causes of high cholesterol were excluded, from PMID 7635461 (Ekstrom et al., 1995), Sweden. BP4: Variant is synonymous and splicing evaluation is required. Functional data on splicing is not available. MES: A) Not on limits. B) Not on limits. Variant is not predicted to alter splicing. SpliceAI did not predict alternative splicing (Δ score=0). BP7 met: Variant is synonymous and meets BP4. This variant has 2 supporting evidence codes (BP4, BP7) towards Benign, enough to classify as Likely Benign, and only PM2 and PP4 evidence codes towards Pathogenic, not enough for Likely Pathogenic, so we are confident in classifying this variant as Likely Benign.

Met criteria codes

BP4			Variant is synonymous and splicing evaluation is required. Functional data on splicing is not available. MES: A) Not on limits. B) Not on limits. Variant is not predicted to alter splicing. SpliceAI did not predict alternative splicing (Δ score=0).
BP7			Variant is synonymous and meets BP4.
PP4			Variant meets PM2 and is identified in 1 index case who fulfils Simon Broome criteria for possible FH diagnosis (Child “K” in Table 1, 10 or 11 years old, LDLC 6 mmol/l and LDLC in one parent $\geq$ +2SD), after alternative causes of high cholesterol were excluded. Ekstrom et al, 1995, reported this case in PMID 7635461, from University of Lund, Sweden.
PM2			PopMax MAF=0.00006 in Latino population in gnomAD (gnomAD v2.1.1).

Curation History [↗](#)







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