

Variant: NM_000527.5(LDLR):c.2017A>C (p.Ser673Arg)

Version: 1.0

CA038161 [↗](#)

252172 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 455c0142-2d2a-44ed-ae97-11feb6cdf45f

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Published on: 2025/6/30

HGVS expressions

NM_000527.5:c.2017A>C

NM_000527.5(LDLR):c.2017A>C (p.Ser673Arg)

NC_000019.10:g.11120399A>C

CM000681.2:g.11120399A>C

NC_000019.9:g.11231075A>C

CM000681.1:g.11231075A>C

NC_000019.8:g.11092075A>C

NG_009060.1:g.36019A>C

ENST00000252444.10:c.2275A>C

ENST00000559340.2:c.*86A>C

ENST00000560467.2:c.1897A>C

ENST00000558518.6:c.2017A>C

ENST00000252444.9:c.2271A>C

ENST00000455727.6:c.1513A>C

ENST00000535915.5:c.1894A>C

ENST00000545707.5:c.1606+166A>C

ENST00000557933.5:c.2017A>C

ENST00000558013.5:c.2017A>C

ENST00000558518.5:c.2017A>C

ENST00000559340.1:c.598A>C

NM_000527.4:c.2017A>C

NM_001195798.1:c.2017A>C

NM_001195799.1:c.1894A>C

NM_001195800.1:c.1513A>C

NM_001195803.1:c.1606+166A>C

NM_001195798.2:c.2017A>C

NM_001195799.2:c.1894A>C

NM_001195800.2:c.1513A>C

NM_001195803.2:c.1606+166A>C

Uncertain Significance

Met criteria codes **1**

PM2

Not Met criteria codes **7**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

PS3

PS4

BP4

PP3

PM1

PM5

BS3

Evidence Links

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[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.2017A>C (p.Ser673Arg) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence code PM2 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= 0.0000008474 (0.00008474%) in European non-Finnish exomes + genomes (gnomAD v.4.1.0).

Met criteria codes

PM2

PopMax MAF= 0.0000008474 (0.00008474%) in European non-Finnish exomes + genomes (gnomAD v.4.1.0).

Not Met criteria codes

PS3

No functional study.

PS4

Variant meets PM2 and is identified in 1 Brazilian FH index with heterozygous FH following WHO criteria from PMID: 11933210. However, the case harbours two LDLR variants c.2017A>C and c.2088C>G and cis/trans status was not determined.

BP4

REVEL = 0.504, it is not below 0.50.

PP3

REVEL = 0.504, it is not below 0.50, splicing evaluation required. A) not on limits B) does not create AG C) there is an AG nearby but splicing scores are negative Variant is not predicted to alter splicing.

PM1

Variant meets PM2 but it is not in exon 4 (located in exon 14) and does not alter a critical Cys residue.

PM5

There is another missense variant in same codon NM_000527.5(LDLR):c.2018G>A (p.Ser673Asn), but not classified as Pathogenic by LDLR guidelines.

BS3

No functional study.

Curation History [↗](#)

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