

*Variant: NM\_000527.5(LDLR):c.1189T>C (p.Ser397Pro)*

Version: 1.0

CA404084655 [↗](#)

923326 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Semidominant inheritance

**UUID:** fcdc1140-e906-4094-ae0a-feca9047e230

**Approved on:** 2023/6/23

**Published on:** 2025/9/16

### *HGVS expressions*

**NM\_000527.5:c.1189T>C**

**NM\_000527.5(LDLR):c.1189T>C (p.Ser397Pro)**

NC\_000019.10:g.11113280T>C

CM000681.2:g.11113280T>C

NC\_000019.9:g.11223956T>C

CM000681.1:g.11223956T>C

NC\_000019.8:g.11084956T>C

NG\_009060.1:g.28900T>C

ENST00000252444.10:c.1447T>C

ENST00000559340.2:c.1189T>C

ENST00000560467.2:c.1069T>C

ENST00000558518.6:c.1189T>C

ENST00000252444.9:c.1443T>C

ENST00000455727.6:c.685T>C

ENST00000535915.5:c.1066T>C

ENST00000545707.5:c.808T>C

ENST00000557933.5:c.1189T>C

ENST00000558013.5:c.1189T>C

ENST00000558518.5:c.1189T>C

ENST00000560173.1:n.188T>C

ENST00000560467.1:c.669T>C

NM\_000527.4:c.1189T>C

NM\_001195798.1:c.1189T>C

NM\_001195799.1:c.1066T>C

NM\_001195800.1:c.685T>C

NM\_001195803.1:c.808T>C

NM\_001195798.2:c.1189T>C

NM\_001195799.2:c.1066T>C

NM\_001195800.2:c.685T>C

NM\_001195803.2:c.808T>C

**Uncertain Significance**

## Met criteria codes **1**

PM2

## Not Met criteria codes 6

PM5

BS1

PS1

BP4

BA1

PP3

Evidence Links 0

## Expert Panel

## Familial Hypercholesterolemia VCEP

## Criteria Specification Information

 **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.1189T>C (p.Ser397Pro) 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 23 June 2023. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v20210610).

Met criteria codes

|     |  |  |                                                        |
|-----|--|--|--------------------------------------------------------|
| PM2 |  |  | This variant is absent from gnomAD (gnomAD v20210610). |
|-----|--|--|--------------------------------------------------------|

Not Met criteria codes

|     |  |  |                                                                                                                                                                                                                                                                                                                                                              |
|-----|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PM5 |  |  | 2 other missense variants in the same codon: - NM_000527.5(LDLR):c.1189T>A (p.Ser397Thr) (ClinVar ID 251725) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.1190C>T (p.Ser397Phe) (ClinVar ID 925475) - Uncertain significance by these guidelines There are no variants in the same codon classified as Pathogenic by these guidelines. |
| BS1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                   |
| PS1 |  |  | There are no variants causing the same amino acid change classified as Pathogenic by these guidelines.                                                                                                                                                                                                                                                       |
| BP4 |  |  | REVEL = 0.502, it is not below 0.50.                                                                                                                                                                                                                                                                                                                         |
| BA1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                   |
| PP3 |  |  | REVEL = 0.502, it is not above 0.75, splicing evaluation required. Functional data on splicing not available. A) Variant within limits MES scores: canonical site variant = 7.47; canonical acceptor wt = 6.59. Ratio: 7.47/6.59 = 1.13---- It is not <0.8. Variant is not predicted to alter splicing                                                       |

Curation History

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