

Variant: *NM\_000527.5(LDLR):c.1761C>G (p.Ser587Arg)*

Version: 1.0

CA036457 [↗](#)

252021 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Semidominant inheritance

**UUID:** 2f2fa622-b260-4dae-8332-c06d4eb16d25

**Approved on:** 2025/3/28

**Published on:** 2025/6/4

### *HGVS expressions*

**NM\_000527.5:c.1761C>G**

**NM\_000527.5(LDLR):c.1761C>G (p.Ser587Arg)**

NC\_000019.10:g.11116914C>G

CM000681.2:g.11116914C>G

NC\_000019.9:g.11227590C>G

CM000681.1:g.11227590C>G

NC\_000019.8:g.11088590C>G

NG\_009060.1:g.32534C>G

ENST00000252444.10:c.2019C>G

ENST00000559340.2:c.1705+702C>G

ENST00000560467.2:c.1641C>G

ENST00000558518.6:c.1761C>G

ENST00000252444.9:c.2015C>G

ENST00000455727.6:c.1257C>G

ENST00000535915.5:c.1638C>G

ENST00000545707.5:c.1380C>G

ENST00000557933.5:c.1761C>G

ENST00000558013.5:c.1761C>G

ENST00000558518.5:c.1761C>G

ENST00000559340.1:c.426+702C>G

NM\_000527.4:c.1761C>G

NM\_001195798.1:c.1761C>G

NM\_001195799.1:c.1638C>G

NM\_001195800.1:c.1257C>G

NM\_001195803.1:c.1380C>G

NM\_001195798.2:c.1761C>G

NM\_001195799.2:c.1638C>G

NM\_001195800.2:c.1257C>G

NM\_001195803.2:c.1380C>G

Uncertain Significance

Met criteria codes **1**

PM2

Not Met criteria codes **11**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

BA1BS2BS1BS4BS3BP4PS3PS4PP1PP3PP4

Evidence Links0

- [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.1761C>G (p.Ser587Arg) 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 = 0.00001356 (0.0014%) in European (non-Finnish) (gnomAD v4.1.0).

Met criteria codes

|     |  |  |                                                                                                               |
|-----|--|--|---------------------------------------------------------------------------------------------------------------|
| PM2 |  |  | PopMax MAF = 0.00001356 (0.0014%) in European (non-Finnish) (gnomAD v4.0). PM2 is met since PopMax MAF<0.02%. |
|-----|--|--|---------------------------------------------------------------------------------------------------------------|

Not Met criteria codes

|     |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BA1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| BS2 |  |  | not met, (no information of index cases or report of segregation data/cases)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| BS1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| BS4 |  |  | not met, (no information of index cases or report of segregation data/cases)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| BS3 |  |  | not met (no information or reports of functional data).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| BP4 |  |  | REVEL = 0.746. REVEL not above 0.75 and not below 0.50. Splicing evaluation is required. Functional data on splicing not available. A) not on limits, B) variant does not creates GT or AG, C) There is an AG nearby (and there is no GT nearby). MES scores: variant cryptic score (TCAAGGATC) = -23.44, wt cryptic (TCAAGCATC) = -32.62, canonical acceptor = 7.93. Ratio variant cryptic/wt cryptic: -23.44/-32.62 = 0.72 --- it is not above 1.1, and Ratio variant cryptic/canonical acceptor: -23.44/7.93= -12.6 --- it is not above 0.9. Therefore, PP3 is not met. |
| PS3 |  |  | not met (no information or reports of functional data).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| PS4 |  |  | not met, (no information of index cases or report of segregation data/cases)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

