

Variant: *NM_000527.5(LDLR):c.2039T>C (p.Leu680Pro)*

Version: 1.0

CA404093609 [↗](#)

440674 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 7682bb41-edcc-47f6-b8f4-5b1f2c9f8d26

Approved on: 2025/7/11

Published on: 2025/10/8

HGVS expressions

NM_000527.5(LDLR):c.2039T>C (p.Leu680Pro)

NM_000527.5:c.2039T>C

NC_000019.10:g.11120421T>C

CM000681.2:g.11120421T>C

NC_000019.9:g.11231097T>C

CM000681.1:g.11231097T>C

NC_000019.8:g.11092097T>C

NG_009060.1:g.36041T>C

ENST00000252444.10:c.2297T>C

ENST00000559340.2:c.*108T>C

ENST00000560467.2:c.1919T>C

ENST00000558518.6:c.2039T>C

ENST00000252444.9:c.2293T>C

ENST00000455727.6:c.1535T>C

ENST00000535915.5:c.1916T>C

ENST00000545707.5:c.1606+188T>C

ENST00000557933.5:c.2039T>C

ENST00000558013.5:c.2039T>C

ENST00000558518.5:c.2039T>C

NM_000527.4:c.2039T>C

NM_001195798.1:c.2039T>C

NM_001195799.1:c.1916T>C

NM_001195800.1:c.1535T>C

NM_001195803.1:c.1606+188T>C

NM_001195798.2:c.2039T>C

NM_001195799.2:c.1916T>C

NM_001195800.2:c.1535T>C

NM_001195803.2:c.1606+188T>C

Uncertain Significance

Met criteria codes **3**

PP3

PP4

PM2

Not Met criteria codes **3**

PP1

PM1

PS4

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.2039T>C (p.Leu680Pro) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PP3 and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 11 July 2025. The supporting evidence is as follows: **PM2:** This variant is absent from gnomAD (gnomAD v4.1.0). **PM3:** REVEL score = 0.918. **PP4:** Variant meets PM2 and is identified in at least 1 index case who fulfills MEDPED criteria for FH from PMID 27824480 (Gabčová et al., 2017), Slovakia, after alternative causes of high cholesterol were excluded.

Met criteria codes

PP3			REVEL score = 0.918 so PP3 is met.
PP4			PP4_Met: Variant meets PM2 and was identified in 2 related patients who fulfil clinical criteria for FH (MEDPED criteria) from PMID: 27824480, after alternative causes of high cholesterol are excluded
PM2			PM2_Met: This variant is absent from gnomAD (gnomAD v4.1.0);

Not Met criteria codes

PP1			PP1_Not Met: the variant was reported in only 1 related (1 informative meiosis) from PMID: 27824480, so PP1 is Not Met.
PM1			PM1_Not Met: variant meets PM2 but it is not located in exon 4 (located in exon 14) and is not affecting one of the highly conserved cysteins, so PM1 is not Met.
PS4			PS4_Not Met: the variant meets PM2 but was identified in 2 related patients who fulfil clinical criteria for FH (MEDPED criteria - PMID: 27824480)

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.