

Variant: *NM_000527.5(LDLR):c.1825T>C (p.Phe609Leu)*

Version: 1.0

CA10585632 [↗](#)

252052 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 627e25c9-32f9-494c-bbbc-e0c679aa740d

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HGVS expressions

NM_000527.5(LDLR):c.1825T>C (p.Phe609Leu)

NM_000527.5:c.1825T>C

NC_000019.10:g.11116978T>C

CM000681.2:g.11116978T>C

NC_000019.9:g.11227654T>C

CM000681.1:g.11227654T>C

NC_000019.8:g.11088654T>C

NG_009060.1:g.32598T>C

ENST00000252444.10:c.2083T>C

ENST00000559340.2:c.1705+766T>C

ENST00000560467.2:c.1705T>C

ENST00000558518.6:c.1825T>C

ENST00000252444.9:c.2079T>C

ENST00000455727.6:c.1321T>C

ENST00000535915.5:c.1702T>C

ENST00000545707.5:c.1444T>C

ENST00000557933.5:c.1825T>C

ENST00000558013.5:c.1825T>C

ENST00000558518.5:c.1825T>C

ENST00000559340.1:c.426+766T>C

NM_000527.4:c.1825T>C

NM_001195798.1:c.1825T>C

NM_001195799.1:c.1702T>C

NM_001195800.1:c.1321T>C

NM_001195803.1:c.1444T>C

NM_001195798.2:c.1825T>C

NM_001195799.2:c.1702T>C

NM_001195800.2:c.1321T>C

NM_001195803.2:c.1444T>C

Uncertain Significance

Met criteria codes **2**

PP4

PM2

Not Met criteria codes **9**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1825T>C (p.Phe609Leu) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying AMCG/AMP evidence codes PM2 and PP4 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: This variant is absent from gnomAD (gnomAD v4.1.0). PP4: Variant meets PM2 and is identified in at least 1 index case fulfilling FH criteria, after alternative causes of high cholesterol were excluded, from PMID 16250003 (Fouchier et al., 2005).

Met criteria codes

PP4			Variant meets PM2 and is identified in at least 1 index case fulfilling FH criteria, after alternative causes of high cholesterol were excluded, from PMID:16250003
PM2			This variant is absent from gnomAD (gnomAD v4.1).

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			REVEL = 0.694. REVEL not above 0.75 and not bellow 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 no AG or GT nearby. Variant is not predicted to alter splicing, so BP4 is not met.
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).
PP1			not met, (no information of index cases or report of segregation data/cases)
PP3			REVEL = 0.694. REVEL not above 0.75 and not bellow 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 no AG or GT nearby. Variant

is not predicted to alter splicing, so 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)

Curation History



Showing 1 to 1 of 1 rows

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