

Variant: *NM_000527.5(LDLR):c.251C>G (p.Pro84Arg)*

Version: 1.0

CA10584810 [↗](#)

251095 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: b6e95616-fb67-494c-b874-db117c6535cc

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HGVS expressions

NM_000527.5(LDLR):c.251C>G (p.Pro84Arg)

NM_000527.5:c.251C>G

NC_000019.10:g.11102724C>G

CM000681.2:g.11102724C>G

NC_000019.9:g.11213400C>G

CM000681.1:g.11213400C>G

NC_000019.8:g.11074400C>G

NG_009060.1:g.18344C>G

ENST00000252444.10:c.509C>G

ENST00000559340.2:c.251C>G

ENST00000560467.2:c.251C>G

ENST00000558518.6:c.251C>G

ENST00000252444.9:c.505C>G

ENST00000455727.6:c.251C>G

ENST00000535915.5:c.190+2379C>G

ENST00000545707.5:c.251C>G

ENST00000557933.5:c.251C>G

ENST00000557958.1:n.337C>G

ENST00000558013.5:c.251C>G

ENST00000558518.5:c.251C>G

NM_000527.4:c.251C>G

NM_001195798.1:c.251C>G

NM_001195799.1:c.190+2379C>G

NM_001195800.1:c.251C>G

NM_001195803.1:c.251C>G

NM_001195798.2:c.251C>G

NM_001195799.2:c.190+2379C>G

NM_001195800.2:c.251C>G

NM_001195803.2:c.251C>G

Uncertain Significance

Met criteria codes **2**

PM2

PP4

Not Met criteria codes **3**

PM5

BP4

PP3

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.251C>G (p.Pro84Arg) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence code PM2 and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (<https://doi.org/10.1016/j.gim.2021.09.012>). The supporting evidence is as follows: PM2 - This variant is absent from gnomAD (gnomAD v2.1.1).: PP4 - Variant meets PM2 and is identified in one index case from PMID 16159606 who fulfill SB criteria for FH.

Met criteria codes

PM2			This variant is absent from gnomAD (gnomAD v2.1.1)
PP4			Variant meets PM2 and is identified in one index case from PMID 16159606 who fulfill SB criteria for FH.

Not Met criteria codes

PM5			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.250C>T (p.Pro84Ser) Uncertain significance - insufficient evidence by these guidelines. - NM_000527.5(LDLR):c.251C>T (p.Pro84Leu) Uncertain significance - insufficient evidence by these guidelines. There are 2 variants in the same codon classified as Uncertain significance - insufficient evidence by these guidelines.
BP4			REVEL = 0.575, it is not below 0.50
PP3			REVEL = 0.575, it is not above 0.75, splicing evaluation required. Functional data on splicing not available. - Variant is exonic and at least 50bp downstream from canonical acceptor site and creates GT. MES scores: de novo variant = 1,62, canonical donor = 9.90. Ratio de novo variant/canonical donor = 1,50/9,90 = 0,15 --- it is not above 0.9 - Variant is exonic and at least 50bp upstream from canonical donor site but it does not create AG. there is no AG nearby

Showing 1 to 1 of 1 rows

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