

Variant: *NM_000527.5(LDLR):c.250C>T (p.Pro84Ser)*

Version: 1.0

CA10584809 [↗](#)

251094 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: c79042aa-3408-4532-83a1-6730dde53e95

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HGVS expressions

NM_000527.5:c.250C>T

NM_000527.5(LDLR):c.250C>T (p.Pro84Ser)

NC_000019.10:g.11102723C>T

CM000681.2:g.11102723C>T

NC_000019.9:g.11213399C>T

CM000681.1:g.11213399C>T

NC_000019.8:g.11074399C>T

NG_009060.1:g.18343C>T

ENST00000252444.10:c.508C>T

ENST00000559340.2:c.250C>T

ENST00000560467.2:c.250C>T

ENST00000558518.6:c.250C>T

ENST00000252444.9:c.504C>T

ENST00000455727.6:c.250C>T

ENST00000535915.5:c.190+2378C>T

ENST00000545707.5:c.250C>T

ENST00000557933.5:c.250C>T

ENST00000557958.1:n.336C>T

ENST00000558013.5:c.250C>T

ENST00000558518.5:c.250C>T

NM_000527.4:c.250C>T

NM_001195798.1:c.250C>T

NM_001195799.1:c.190+2378C>T

NM_001195800.1:c.250C>T

NM_001195803.1:c.250C>T

NM_001195798.2:c.250C>T

NM_001195799.2:c.190+2378C>T

NM_001195800.2:c.250C>T

NM_001195803.2:c.250C>T

Uncertain Significance

Met criteria codes **2**

PP4

PM2

Not Met criteria codes **3**

BP4

PP3

PM5

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.250C>T (p.Pro84Ser) 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 who fulfill FH/DLCN>=6 criteria for FH from PMID 11810272

Met criteria codes

PP4			PP4 - Variant meets PM2 and is identified in one index case who fulfill FH/DLCN>=6 criteria for FH from PMID 11810272
PM2			This variant is absent from gnomAD (gnomAD v2.1.1)

Not Met criteria codes

BP4			REVEL = 0.622, it is not below 0.50
PP3			REVEL = 0.622, 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 but it does not create GT. - There is a GT nearby. MES scores: variant cryptic = -38.14, wt cryptic = -37.91, canonical donor = 9.90. Ratio variant cryptic/wt cryptic: -38.14/-37,91 = 1,01 --- it is not above 1.1 Ratio variant cryptic/canonical donor: -38,14/9,90 = -3,85 --- 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
PM5			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.251C>G (p.Pro84Arg) 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.

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