

Variant: NM_000527.5(LDLR):c.1244A>T (p.Asp415Val)

Version: 1.0

CA10585373 [↗](#)

251750 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 1917847c-1383-4ebb-9c3d-b2954f97e777

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HGVS expressions

NM_000527.5:c.1244A>T

NM_000527.5(LDLR):c.1244A>T (p.Asp415Val)

NC_000019.10:g.11113335A>T

CM000681.2:g.11113335A>T

NC_000019.9:g.11224011A>T

CM000681.1:g.11224011A>T

NC_000019.8:g.11085011A>T

NG_009060.1:g.28955A>T

ENST00000252444.10:c.1502A>T

ENST00000559340.2:c.1244A>T

ENST00000560467.2:c.1124A>T

ENST00000558518.6:c.1244A>T

ENST00000252444.9:c.1498A>T

ENST00000455727.6:c.740A>T

ENST00000535915.5:c.1121A>T

ENST00000545707.5:c.863A>T

ENST00000557933.5:c.1244A>T

ENST00000558013.5:c.1244A>T

ENST00000558518.5:c.1244A>T

ENST00000560173.1:n.243A>T

ENST00000560467.1:c.724A>T

NM_000527.4:c.1244A>T

NM_001195798.1:c.1244A>T

NM_001195799.1:c.1121A>T

NM_001195800.1:c.740A>T

NM_001195803.1:c.863A>T

NM_001195798.2:c.1244A>T

NM_001195799.2:c.1121A>T

NM_001195800.2:c.740A>T

NM_001195803.2:c.863A>T

Uncertain Significance

Met criteria codes 3

Not Met criteria codes 1

Evidence Links 0

PP3PM3PM2

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.1244A>T (p.Asp415Val) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PM3 and PP3 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 23 June 2023. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v2.1.1). PP3: REVEL = 0.929. PM3: 1 case reported in PMID 36325061 (Du et al., 2022), China, who was homozygous and presented with an untreated LDL-C ≥13 mmol/L or a treated LDL-C ≥8 mmol/L and either cutaneous or tendon xanthomas before the age of 10 years.

Met criteria codes

PP3

- PP3: REVEL = 0.929. It is above 0.75, so PP3 is met.

PM3

- PM3: 1 case reported in PMID 36325061, who is true homozygous and presents an untreated LDL-C ≥ 13 mmol/L or a treated LDL-C ≥ 8 mmol/L, either cutaneous or tendon xanthomas before the age of 10 years. PM3 is met.

PM2

- PM2: This variant is absent from gnomAD (gnomAD v2.1.1).

Not Met criteria codes

PM5

NM_000527.5(LDLR):c.1244A>G (p.Asp415Gly) (ClinVar ID: 251749) considered as Likely Pathogenic by these guidelines. NM_000527.5(LDLR):c.1243G>C (p.Asp415His) (ClinVar ID: 251748) considered as Likely Pathogenic by these guidelines.

Curation History

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