

Variant: NM_000527.5(LDLR):c.921T>G (p.Asp307Glu)

Version: 1.0

CA10585197 [↗](#)

251527 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: ea10f4d0-8b80-469c-a9cc-ea74084ade69

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HGVS expressions

NM_000527.5(LDLR):c.921T>G (p.Asp307Glu)

NM_000527.5:c.921T>G

NC_000019.10:g.11107495T>G

CM000681.2:g.11107495T>G

NC_000019.9:g.11218171T>G

CM000681.1:g.11218171T>G

NC_000019.8:g.11079171T>G

NG_009060.1:g.23115T>G

ENST00000252444.10:c.1179T>G

ENST00000559340.2:c.921T>G

ENST00000560467.2:c.921T>G

ENST00000558518.6:c.921T>G

ENST00000252444.9:c.1175T>G

ENST00000455727.6:c.417T>G

ENST00000535915.5:c.798T>G

ENST00000545707.5:c.540T>G

ENST00000557933.5:c.921T>G

ENST00000558013.5:c.921T>G

ENST00000558518.5:c.921T>G

ENST00000558528.1:n.436T>G

ENST00000560467.1:c.521T>G

NM_000527.4:c.921T>G

NM_001195798.1:c.921T>G

NM_001195799.1:c.798T>G

NM_001195800.1:c.417T>G

NM_001195803.1:c.540T>G

NM_001195798.2:c.921T>G

NM_001195799.2:c.798T>G

NM_001195800.2:c.417T>G

NM_001195803.2:c.540T>G

Uncertain Significance

Met criteria codes 4

PP3PP4PM2PS4_Supporting

Not Met criteria codes 1

PM5

Evidence Links 0

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.921T>G (p.Asp307Glu) variant is classified as VUS for Familial Hypercholesterolemia by applying evidence codes PM2, PP3, and PP4 and PS4_Supporting 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). PP3: REVEL = 0.85. PP4: Variant meets PM2 and is identified in at least 1 index case who fulfills SB definite FH after alternative causes of high cholesterol were excluded (PMID: 12436241). PS4_Supporting: Variant meets PM2 and is identified in at least 2 unrelated index cases who fulfill SB definite FH/DLCN>=6 for FH (PMID: 12436241, Lille University SCV000583761.1).

Met criteria codes

PP3

REVEL = 0.85.

PP4

Variant meets PM2 and is identified in at least 1 index case who fulfills SB definite FH after alternative causes of high cholesterol were excluded (PMID: 12436241).

PM2

This variant is absent from gnomAD (gnomAD v2.1.1).

PS4_Supporting

Variant meets PM2 and is identified in at least 2 unrelated index cases who fulfill SB definite FH/DLCN>=6 for FH (PMID: 12436241, Lille University SCV000583761.1)

Not Met criteria codes

PM5

Two other missense variants in the same codon: - NM_000527.5(LDLR):c.920A>G (p.Asp307Gly) - NM_000527.5(LDLR):c.919G>A (p.Asp307Asn) - Likely Pathogenic by these guidelines There are two variants in the same codon classified as Likely Pathogenic (minimum 2) by these guidelines.

Curation History

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