

Variant: NM_000527.5(LDLR):c.919G>A (p.Asp307Asn)

Version: 1.0

CA10585195 [↗](#)

251525 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: cf0f1462-116a-46ff-b154-665b3d799556

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HGVS expressions

NM_000527.5(LDLR):c.919G>A (p.Asp307Asn)

NM_000527.5:c.919G>A

NC_000019.10:g.11107493G>A

CM000681.2:g.11107493G>A

NC_000019.9:g.11218169G>A

CM000681.1:g.11218169G>A

NC_000019.8:g.11079169G>A

NG_009060.1:g.23113G>A

ENST00000252444.10:c.1177G>A

ENST00000559340.2:c.919G>A

ENST00000560467.2:c.919G>A

ENST00000558518.6:c.919G>A

ENST00000252444.9:c.1173G>A

ENST00000455727.6:c.415G>A

ENST00000535915.5:c.796G>A

ENST00000545707.5:c.538G>A

ENST00000557933.5:c.919G>A

ENST00000558013.5:c.919G>A

ENST00000558518.5:c.919G>A

ENST00000558528.1:n.434G>A

ENST00000560467.1:c.519G>A

NM_000527.4:c.919G>A

NM_001195798.1:c.919G>A

NM_001195799.1:c.796G>A

NM_001195800.1:c.415G>A

NM_001195803.1:c.538G>A

NM_001195798.2:c.919G>A

NM_001195799.2:c.796G>A

NM_001195800.2:c.415G>A

NM_001195803.2:c.538G>A

Likely Pathogenic

Met criteria codes 5

PS4_ModeratePP3PP4PM2

PP1_Moderate

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.919G>A (p.Asp307Asn) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying evidence codes PP1_Moderate, PM2, PS4_Moderate, PP3 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: PP1_Moderate: Variant segregates with FH phenotype in at least 5 informative meioses from 2 different families (PMID: 32706999, Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)). PM2: This variant is absent from gnomAD (gnomAD v2.1.1). PS4_Moderate:Variant meets PM2 and is identified in at least 6 unrelated index cases who fulfill SB possible or definite criteria for FH from different labs (PMID: 32706999, Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)). PP3: REVEL = 0.865 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: 32706999).

Met criteria codes

PS4_Moderate			Variant meets PM2 and is identified in at least 6 unrelated index cases who fulfill SB possible or definite criteria for FH from different labs (PMID: 32706999, Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)).
PP3			REVEL = 0.865
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: 32706999).
PM2			This variant is absent from gnomAD (gnomAD v2.1.1).
PP1_Moderate			Variant segregates with FH phenotype in at least 5 informative meioses from 2 different families (PMID: 32706999, Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)).

Not Met criteria codes

PM5			One other missense variant in the same codon: - NM_000527.5(LDLR):c.920A>G (p.Asp307Gly) - Likely Pathogenic by these guidelines There is 1 variant in the same codon classified as Likely Pathogenic by these guidelines.
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Curation History



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