

Variant: *NM_000527.5(LDLR):c.169G>A (p.Asp57Asn)*

Version: 1.0

[CA10584771](#) 

[251040 \(ClinVar\)](#) 

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

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

Inheritance Mode: Semidominant inheritance

UUID: 7db92565-5287-495d-97ef-45a26dd534ac

Approved on: 2022-08-29

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HGVS expressions

NM_000527.5:c.169G>A

NM_000527.5(LDLR):c.169G>A (p.Asp57Asn)

NC_000019.10:g.11100324G>A

CM000681.2:g.11100324G>A

NC_000019.9:g.11211000G>A

CM000681.1:g.11211000G>A

NC_000019.8:g.11072000G>A

NG_009060.1:g.15944G>A

ENST00000252444.10:c.427G>A

ENST00000559340.2:c.169G>A

ENST00000560467.2:c.169G>A

ENST00000558518.6:c.169G>A

ENST00000252444.9:c.423G>A

ENST00000455727.6:c.169G>A

ENST00000535915.5:c.169G>A

ENST00000545707.5:c.169G>A

ENST00000557933.5:c.169G>A

ENST00000557958.1:n.255G>A

ENST00000558013.5:c.169G>A

ENST00000558518.5:c.169G>A

ENST00000560502.5:n.255G>A

NM_000527.4:c.169G>A

NM_001195798.1:c.169G>A

NM_001195799.1:c.169G>A

NM_001195800.1:c.169G>A

NM_001195803.1:c.169G>A

NM_001195798.2:c.169G>A

NM_001195799.2:c.169G>A

NM_001195800.2:c.169G>A

NM_001195803.2:c.169G>A

Uncertain Significance

Met criteria codes **3**

PP3 PP4 PM2

Not Met criteria codes **10**

Expert Panel

[Familial Hypercholesterolemia VCEP](#) 

Criteria Specification Information 

PS1 PS3 PVS1 PM5 PM4
BA1 BS1 BS3 BP4 BP3

[Criteria Specifications for this VCEP](#)

Evidence Links **0**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.169G>A (p.Asp57Asn) variant is classified as **Uncertain significance - insufficient evidence for Familial Hypercholesterolemia** by applying evidence codes **PM2, 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: **PM2: This variant is absent from gnomAD (gnomAD v2.1.1.). So PM2 is met. PP3: REVEL= 0.791. It is above 0.75, so PP3 is met. PP4: Variant meets PM2 and is identified in 1 case fulfilling WHO criteria published in PMID: 20145306 (Chmara et al., 2010). So PP4 is met.**

Met criteria codes

| | | |
|------------|---|---|
| PP3 | ✓ | REVEL= 0.791. It is above 0.75, so PP3 is met. |
| PP4 | ✓ | Variant meets PM2 and is identified in 1 case fulfilling WHO criteria published in PMID: 20145306 (Chmara et al., 2010). So PP4 is met. |
| PM2 | ✓ | This variant is absent from gnomAD (gnomAD v2.1.1.). So PM2 is met. |

Not Met criteria codes

| | | |
|-------------|---|---|
| PS1 | ✗ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| PS3 | ✗ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| PVS1 | ✗ | Not a null variant |
| PM5 | ✗ | Two other missense variants in the same codon: -NM_000527.5(LDLR):c.170A>G (p.Asp57Gly) (ClinVar ID 1380181) Uncertain significance by these guidelines -NM_000527.5(LDLR):c.170A>C (p.Asp57Ala) (ClinVar ID 523722) Uncertain significance by these guidelines |
| PM4 | ✗ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| BA1 | ✗ | This variant is absent from gnomAD (gnomAD v2.1.1.). |
| BS1 | ✗ | This variant is absent from gnomAD (gnomAD v2.1.1.). |
| BS3 | ✗ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| BP4 | ✗ | REVEL= 0.791. It is above 0.5 |
| BP3 | ✗ | |

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History [↗](#)



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| View Report | Preferred Variant Title | Classification ⓘ | Condition | Published Date | Version ⓘ | Criteria Specification | Gene |
|-----------------------------|---|----------------------------------|--|--------------------------------|---------------------------|--|------------------------|
| View | NM_000527.5(LDLR):c.169G>A (p.Asp5... | Uncertain Significance | Hypercholesterolemia, Familial ↗ | 2022-12-23 | 1.0 | - | LDLR ↗ |

Showing 1 to 1 of 1 rows

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