

Variant: *NM\_000527.5(LDLR):c.1765G>A (p.Asp589Asn)*

Version: 1.0

[CA036508](#)

[252022 \(ClinVar\)](#)

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

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

**Inheritance Mode:** Semidominant inheritance

**UUID:** fd0cb6c9-7f1e-4644-9c34-95083a79a553

**Approved on:** 2022-08-29

**Published on:** 2022-12-23

### *HGVS expressions*

**NM\_000527.5:c.1765G>A**

NM\_000527.5(LDLR):c.1765G>A (p.Asp589Asn)

NC\_000019.10:g.11116918G>A

CM000681.2:g.11116918G>A

NC\_000019.9:g.11227594G>A

CM000681.1:g.11227594G>A

NC\_000019.8:g.11088594G>A

NG\_009060.1:g.32538G>A

ENST00000252444.10:c.2023G>A

ENST00000559340.2:c.1705+706G>A

ENST00000560467.2:c.1645G>A

ENST00000558518.6:c.1765G>A

ENST00000252444.9:c.2019G>A

ENST00000455727.6:c.1261G>A

ENST00000535915.5:c.1642G>A

ENST00000545707.5:c.1384G>A

ENST00000557933.5:c.1765G>A

ENST00000558013.5:c.1765G>A

ENST00000558518.5:c.1765G>A

ENST00000559340.1:c.426+706G>A

NM\_000527.4:c.1765G>A

NM\_001195798.1:c.1765G>A

NM\_001195799.1:c.1642G>A

NM\_001195800.1:c.1261G>A

NM\_001195803.1:c.1384G>A

NM\_001195798.2:c.1765G>A

NM\_001195799.2:c.1642G>A

NM\_001195800.2:c.1261G>A

NM\_001195803.2:c.1384G>A

Uncertain Significance

Met criteria codes **1**

BP4

Not Met criteria codes **4**

BP5

PS4

PM5

PM2

Expert Panel

[Familial Hypercholesterolemia VCEP](#)

Criteria Specification Information

## Evidence submitted by expert panel

***Familial Hypercholesterolemia VCEP***

The NM\_000527.5(LDLR):c.1765G>A (p.Asp589Asn) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes BP4 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: BP4 - REVEL = 0.325. It is below 0.5, splicing evaluation needed. Functional data on splicing not available. A) variant not on limits. B) does not create AG or GT Variant is not predicted to alter splicing

**Met criteria codes**

<b>BP4</b>	<span style="color: green;">✔</span>	BP4 - REVEL = 0.325. It is below 0.5, splicing evaluation needed. Functional data on splicing not available. A) variant not on limits. B) does not create AG or GT Variant is not predicted to alter splicing
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**Not Met criteria codes**

<b>BP5</b>	<span style="color: red;">✘</span>	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS4</b>	<span style="color: red;">✘</span>	MAF = 0.105% in East Asians
<b>PM5</b>	<span style="color: red;">✘</span>	2 other variants in the same codon but both are classified as VUS per ClinGen LDLR VCEP guidelines
<b>PM2</b>	<span style="color: red;">✘</span>	PM2 - PopMax MAF = 0.001053 (0.11%) in East-Asian European exomes/genomes (gnomAD v2.1.1).

Curation History [↗](#)

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