

Variant: *NM\_000527.5(LDLR):c.1721G>A (p.Arg574His)*

Version: 1.1

CA036197 [↗](#)

251996 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Semidominant inheritance

**UUID:** 4eae98db-aaea-4688-83be-718337c06f12

**Approved on:** 2022-02-13

**Published on:** 2022-07-12

### *HGVS expressions*

#### **NM\_000527.5:c.1721G>A**

NM\_000527.5(LDLR):c.1721G>A (p.Arg574His)

NC\_000019.10:g.11116874G>A

CM000681.2:g.11116874G>A

NC\_000019.9:g.11227550G>A

CM000681.1:g.11227550G>A

NC\_000019.8:g.11088550G>A

NG\_009060.1:g.32494G>A

ENST00000252444.10:c.1979G>A

ENST00000559340.2:c.1705+662G>A

ENST00000560467.2:c.1601G>A

ENST00000558518.6:c.1721G>A

ENST00000252444.9:c.1975G>A

ENST00000455727.6:c.1217G>A

ENST00000535915.5:c.1598G>A

ENST00000545707.5:c.1340G>A

ENST00000557933.5:c.1721G>A

ENST00000558013.5:c.1721G>A

ENST00000558518.5:c.1721G>A

ENST00000559340.1:c.426+662G>A

NM\_000527.4:c.1721G>A

NM\_001195798.1:c.1721G>A

NM\_001195799.1:c.1598G>A

NM\_001195800.1:c.1217G>A

NM\_001195803.1:c.1340G>A

NM\_001195798.2:c.1721G>A

NM\_001195799.2:c.1598G>A

NM\_001195800.2:c.1217G>A

NM\_001195803.2:c.1340G>A

**Likely Pathogenic**

Met criteria codes **4**

PM2 PP1\_Strong PP3 PP4

Not Met criteria codes **22**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

[BA1](#) [PM6](#) [PM1](#) [PM3](#) [PM5](#)  
[PM4](#) [BS1](#) [BS4](#) [BS3](#) [PVS1](#)  
[BS2](#) [BP5](#) [BP7](#) [BP4](#) [BP3](#) [BP1](#)  
[BP2](#) [PS1](#) [PS2](#) [PS3](#) [PS4](#) [PP2](#)

Evidence Links 0

[Criteria Specification: ClinGen Familial Hypercholesterolemia Expert Panel Specifications to the ACMG/AMP Variant Classification Guidelines Version 1.1](#)









[PDF](#)  
[Criteria Specification Approval History](#)  
[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel







**Familial Hypercholesterolemia VCEP**

**NM\_000527.5(LDLR):c.1721G>A (p.Arg574His) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PP1\_strong, 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: PP1\_strong - PMID: 20018285 - 6 informative meioses in 1 family. PM2 - PopMax MAF = 0.0001129 (0.01129%) in Latino exomes+genomes (gnomAD v2.1.1). PP3 - REVEL = 0.971. PP4 - Variant meets PM2. PMID: 20018285 - 1 case with DLCN > 6.**





























**Met criteria codes**







<b>PM2</b>			PopMax MAF = 0.0001129 (0.01129%) in Latino exomes+genomes (gnomAD v2.1.1).
<b>PP1_Strong</b>			PMID: 20018285 - 6 informative meioses in 1 family
<b>PP3</b>			REVEL = 0.971
<b>PP4</b>			Variant meets PM2. PMID: 20018285 - 1 case with DLCN > 6.

**Not Met criteria codes**

<b>BA1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PM6</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PM1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PM3</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PM5</b>			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.1720C>T (p.Arg574Cys) (ClinVar ID 183123) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.1721G>T (p.Arg574Leu) (ClinVar ID 237867) -

Uncertain significance by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.



<b>PM4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS3</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PVS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP5</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP7</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP3</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

<b>PS3</b>	 	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS4</b>	 	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PP2</b>	 	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
<a href="#">View</a>	NM_000527.5(LDLR):c.1721G>A (p.Arg...)	<b>Likely Pathogenic</b>	Hypercholesterolemia, Familial <a href="#">↗</a>	2022-07-12	1.1	ClinGen Familial Hypercholesterolemia Expert Panel Specifications to the ACMG/AMP Variant Classification Guidelines Version 1.1 <a href="#">↗</a>	LDLR <a href="#">↗</a>
<a href="#">View</a>	NM_000527.5(LDLR):c.1721G>A (p.Arg...)	<b>Likely Pathogenic</b>	Hypercholesterolemia, Familial <a href="#">↗</a>	2022-03-30	1.0	-	LDLR <a href="#">↗</a>

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