

Variant: NM_000527.5(LDLR):c.241C>A (p.Arg81Ser)

Version: 1.0

CA10584803 [↗](#)

251088 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: b0a05e74-6a94-48ff-887d-e2beff2848ba

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HGVS expressions

NM_000527.5:c.241C>A

NM_000527.5(LDLR):c.241C>A (p.Arg81Ser)

NC_000019.10:g.11102714C>A

CM000681.2:g.11102714C>A

NC_000019.9:g.11213390C>A

CM000681.1:g.11213390C>A

NC_000019.8:g.11074390C>A

NG_009060.1:g.18334C>A

ENST00000252444.10:c.499C>A

ENST00000559340.2:c.241C>A

ENST00000560467.2:c.241C>A

ENST00000558518.6:c.241C>A

ENST00000252444.9:c.495C>A

ENST00000455727.6:c.241C>A

ENST00000535915.5:c.190+2369C>A

ENST00000545707.5:c.241C>A

ENST00000557933.5:c.241C>A

ENST00000557958.1:n.327C>A

ENST00000558013.5:c.241C>A

ENST00000558518.5:c.241C>A

NM_000527.4:c.241C>A

NM_001195798.1:c.241C>A

NM_001195799.1:c.190+2369C>A

NM_001195800.1:c.241C>A

NM_001195803.1:c.241C>A

NM_001195798.2:c.241C>A

NM_001195799.2:c.190+2369C>A

NM_001195800.2:c.241C>A

NM_001195803.2:c.241C>A

Uncertain Significance

Met criteria codes **2**

PP4

PM2

Not Met criteria codes **24**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

BS2

PVS1

BS1

BS4

BS3

BP4

BP3

BP1

BP2

BP5

BP7

PS1

PS2

PS3

PS4

BA1

PP1

PP2

PP3

PM1

PM3

PM5

PM4

PM6

Evidence Links

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- 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.241C>A (p.Arg81Ser) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes PM2 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 (v2.1.1). PP4 - Variant meet PM2. PMID: 21382890 (Graaf et al., 2011) - 1 case with LDL-C level >95th percentile for age and gender and autosomal dominant inheritance pattern of hypercholesterolemia, ie, at least 1 biological parent on treatment for hypercholesterolemia and a family history of hypercholesterolemia and cardiovascular disease. Alternative causes of high cholesterol were excluded.

Met criteria codes

PP4			Variant meet PM2. PMID: 21382890 (Graaf et al., 2011) - 1 case with LDL-C level >95th percentile for age and gender and autosomal dominant inheritance pattern of hypercholesterolemia, ie, at least 1 biological parent on treatment for hypercholesterolemia and a family history of hypercholesterolemia and cardiovascular disease. Alternative causes of high cholesterol were excluded.
PM2			This variant is absent from gnomAD (v2.1.1)

Not Met criteria codes

BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP4			REVEL = 0.669
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			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
PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			REVEL = 0.669
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			

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

PM5			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.242G>A (p.Arg81His)(ClinVar ID 924271) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.241C>T (p.Arg81Cys)(ClinVar ID 183083) - Likely pathogenic by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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