

Variant: *NM_000527.5(LDLR):c.305A>C (p.Gln102Pro)*

Version: 1.0

CA10584836 [↗](#)

251127 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: d4dc86ba-b9d7-433f-a758-0af1ddfb4ac7

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HGVS expressions

NM_000527.5(LDLR):c.305A>C (p.Gln102Pro)

NM_000527.5:c.305A>C

NC_000019.10:g.11102778A>C

CM000681.2:g.11102778A>C

NC_000019.9:g.11213454A>C

CM000681.1:g.11213454A>C

NC_000019.8:g.11074454A>C

NG_009060.1:g.18398A>C

ENST00000252444.10:c.563A>C

ENST00000559340.2:c.305A>C

ENST00000560467.2:c.305A>C

ENST00000558518.6:c.305A>C

ENST00000252444.9:c.559A>C

ENST00000455727.6:c.305A>C

ENST00000535915.5:c.190+2433A>C

ENST00000545707.5:c.305A>C

ENST00000557933.5:c.305A>C

ENST00000557958.1:n.391A>C

ENST00000558013.5:c.305A>C

ENST00000558518.5:c.305A>C

NM_000527.4:c.305A>C

NM_001195798.1:c.305A>C

NM_001195799.1:c.190+2433A>C

NM_001195800.1:c.305A>C

NM_001195803.1:c.305A>C

NM_001195798.2:c.305A>C

NM_001195799.2:c.190+2433A>C

NM_001195800.2:c.305A>C

NM_001195803.2:c.305A>C

Uncertain Significance

Met criteria codes **2**

PM2

PP4

Not Met criteria codes **24**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

PM1

PM3

PM5

PM4

PM6

BS1

BS4

BS3

BS2

PVS1

PS1

PS2

PS3

PS4

BP5

BP7

BP4

BP3

BP1

BP2

BA1

PP1

PP2

PP3

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.305A>C (p.Gln102Pro) 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 (gnomAD v2.1.1). PP4 - Variant meets PM2 and is identified in at least one case who fufills clinical criteria for FH (see PS4 for details), after alternative causes of high cholesterol were excluded.

Met criteria codes

PM2			This variant is absent from gnomAD (gnomAD v2.1.1).
PP4			Variant meets PM2 and is identified in at least one case who fufills clinical criteria for FH (see PS4 for details), after alternative causes of high cholesterol were excluded.

Not Met criteria codes

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			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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
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
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
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
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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 = 0.652, it is not above 0.75, splicing evaluation required. Scenario A, Acceptor site: The variant is not located at -20 to +3 bases of canonical acceptor splicing site of any exons. Scenario A, Donor site: The variant is not located at -3 to +6 bases of canonical splicing site of any exons. Scenario B, Acceptor site: The variant is not located within the range and does not create de novo AG site. Scenario B, Donor site: The variant is located within range and does not create de novo GT site. Scenario C, Acceptor site: The variant is not located at -20 to +3 bases of intraexonic AG. Scenario C, Donor site: The variant is not located at -3 to +6 bases of intraexonic GT. Interpretation: The variant does not affect splicing.

Curation History 	
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