

Variant: NM_000527.5(LDLR):c.139G>C (p.Asp47His)

Version: 1.1

CA404074850 [↗](#)

440546 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 67b39111-3008-4f7c-ad1e-56534ac6aeb8

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HGVS expressions

NM_000527.5(LDLR):c.139G>C (p.Asp47His)

NM_000527.5:c.139G>C

NC_000019.10:g.11100294G>C

CM000681.2:g.11100294G>C

NC_000019.9:g.11210970G>C

CM000681.1:g.11210970G>C

NC_000019.8:g.11071970G>C

NG_009060.1:g.15914G>C

ENST00000252444.10:c.397G>C

ENST00000559340.2:c.139G>C

ENST00000560467.2:c.139G>C

ENST00000558518.6:c.139G>C

ENST00000252444.9:c.393G>C

ENST00000455727.6:c.139G>C

ENST00000535915.5:c.139G>C

ENST00000545707.5:c.139G>C

ENST00000557933.5:c.139G>C

ENST00000557958.1:n.225G>C

ENST00000558013.5:c.139G>C

ENST00000558518.5:c.139G>C

ENST00000560502.5:n.225G>C

NM_000527.4:c.139G>C

NM_001195798.1:c.139G>C

NM_001195799.1:c.139G>C

NM_001195800.1:c.139G>C

NM_001195803.1:c.139G>C

NM_001195798.2:c.139G>C

NM_001195799.2:c.139G>C

NM_001195800.2:c.139G>C

NM_001195803.2:c.139G>C

Uncertain Significance

Met criteria codes 2

PM2

PP3

Not Met criteria codes 24

BP5

BP7

BP4

BP3

BP1

BP2

PM6

PVS1

PM1

PM3

PM5

PM4

BA1

PS1

PS2

PS3

PS4

PP1

PP2

PP4

BS1

BS4

BS3

BS2

Evidence Links 0

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

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

The NM_000527.5(LDLR):c.139G>C (p.Asp47His) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes (PM2 and PP3) as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (<https://doi.org/10.1101/2021.03.17.21252755>) The supporting evidence is as follows: PM2 - This variant is absent from gnomAD (gnomAD v2.1.1). PP3 - REVEL = 0.977. It is above 0.75, so met.

Met criteria codes

PM2		✓	This variant is absent from gnomAD (gnomAD v2.1.1).
PP3		✓	REVEL = 0.977. It is above 0.75, so met.

Not Met criteria codes

BP5		✗	not applicable
BP7		✗	variant is missense, so not applicable
BP4		✗	REVEL = 0.977. It is not below 0.50, so not met
BP3		✗	not applicable
BP1		✗	not applicable
BP2		✗	there is no case data available for this variant
PM6		✗	there is no case data available for this variant

PVS1			variant is missense and not in initiation codon, so not applicable
PM1			variant is missense and meets PM2, but it is not in exon 4 and does not alter Cys, so not met
PM3			there is no case data available for this variant
PM5			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.139G>T (p.Asp47Tyr) - VUS by these guidelines - NM_000527.5(LDLR):c.139G>A (p.Asp47Asn) - VUS by expert panel on ClinVar so not met
PM4			variant is missense, so not applicable
BA1			This variant is absent from gnomAD (gnomAD v2.1.1).
PS1			no other missense variant leads to the same amino acid change, so not met
PS2			there is no case data available for this variant
PS3			variant was not studied in functional studies, so not met
PS4			there is no case data available for this variant
PP1			there is no case data available for this variant
PP2			not applicable
PP4			there is no case data available for this variant
BS1			This variant is absent from gnomAD (gnomAD v2.1.1).
BS4			there is no case data available for this variant
BS3			variant was not studied in functional studies, so not met
BS2			there is no case data available for this variant

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