

Variant: NM_000527.5(LDLR):c.770G>C (p.Arg257Pro)

Version: 1.0

CA404079930 [↗](#)

440602 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 904d2a2f-31e6-4db5-904e-e74c4a7cfd07

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HGVS expressions

NM_000527.5(LDLR):c.770G>C (p.Arg257Pro)

NM_000527.5:c.770G>C

NC_000019.10:g.11106640G>C

CM000681.2:g.11106640G>C

NC_000019.9:g.11217316G>C

CM000681.1:g.11217316G>C

NC_000019.8:g.11078316G>C

NG_009060.1:g.22260G>C

ENST00000252444.10:c.1028G>C

ENST00000559340.2:c.770G>C

ENST00000560467.2:c.770G>C

ENST00000558518.6:c.770G>C

ENST00000252444.9:c.1024G>C

ENST00000455727.6:c.314-752G>C

ENST00000535915.5:c.647G>C

ENST00000545707.5:c.389G>C

ENST00000557933.5:c.770G>C

ENST00000558013.5:c.770G>C

ENST00000558518.5:c.770G>C

ENST00000558528.1:n.285G>C

ENST00000560467.1:c.370G>C

NM_000527.4:c.770G>C

NM_001195798.1:c.770G>C

NM_001195799.1:c.647G>C

NM_001195800.1:c.314-752G>C

NM_001195803.1:c.389G>C

NM_001195798.2:c.770G>C

NM_001195799.2:c.647G>C

NM_001195800.2:c.314-752G>C

NM_001195803.2:c.389G>C

Uncertain Significance

Met criteria codes 1

PM2

Not Met criteria codes 21

BA1 BS2 BS1 BS4 BS3 BP3

BP2 PVS1 BP5 BP7 PS1

PS2 PS3 PS4 PP1 PP4 PM1

PM3 PM5 PM4 PM6

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 1.2](#)

[PDF](#)

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.770G>C (p.Arg257Pro) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence code PM2 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 was not identified in gnomAD (gnomAD v2.1.1).

Met criteria codes

PM2		✓	This variant was not identified in gnomAD (gnomAD v2.1.1)
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Not Met criteria codes

BA1		✗	This variant was not identified in gnomAD (gnomAD v2.1.1)
BS2		✗	there are no reports of this variant being identified in normolipidemic individuals, so not met
BS1		✗	This variant was not identified in gnomAD (gnomAD v2.1.1)
BS4		✗	there are no segregation data, so not met
BS3		✗	there are no functional studies for this variant
BP3		✗	not applicable
BP2		✗	there are no reports of this variant being identified in index cases with other variants, so not met
PVS1		✗	variant is missense and not in initiation codon, so not met

BP5			not applicable
BP7			variant is missense, so not met
PS1			There are no other variants that lead to the same amino acid change, so not met
PS2			there are no reports of this variant being identified de novo, so not met
PS3			there are no functional studies for this variant
PS4			there are no reports of this variant being identified in index cases who fulfill clinical FH criteria, so not met
PP1			there are no segregation data, so not met
PP4			there are no reports of this variant being identified in index cases who fulfill clinical FH criteria, so not met
PM1			variant is missense and meets PM2, but it is not in exon 4 nor does it change Cys, so not met
PM3			there are no reports of this variant being identified in index cases with other variants, so not met
PM5			There are 4 other missense variants in the same codon: NM_000527.5(LDLR):c.769C>T (p.Arg257Trp) (ClinVar ID: 251446) - classified as VUS by these guidelines NM_000527.5(LDLR):c.770_771delinsAC (p.Arg257His) (ClinVar ID: 183094) - classified as VUS by these guidelines NM_000527.5(LDLR):c.770G>A (p.Arg257Gln) (ClinVar ID: 927149) - classified as VUS by these guidelines NM_000527.5(LDLR):c.770G>T (p.Arg257Leu) (ClinVar ID: 251447) - classified as VUS by these guidelines so PM5 is not met
PM4			variant is missense, so not met
PM6			there are no reports of this variant being identified de novo, so not met

Curation History 		
Showing 1 to 1 of 1 rows		

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