

Variant: *NM_000527.5(LDLR):c.551G>C (p.Cys184Ser)*

Version: 1.0

CA404077216 [↗](#)

430757 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: d9517669-3e31-4a47-97e4-371c831bb36d

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HGVS expressions

NM_000527.5:c.551G>C

NM_000527.5(LDLR):c.551G>C (p.Cys184Ser)

NC_000019.10:g.11105457G>C

CM000681.2:g.11105457G>C

NC_000019.9:g.11216133G>C

CM000681.1:g.11216133G>C

NC_000019.8:g.11077133G>C

NG_009060.1:g.21077G>C

ENST00000252444.10:c.809G>C

ENST00000559340.2:c.551G>C

ENST00000560467.2:c.551G>C

ENST00000558518.6:c.551G>C

ENST00000252444.9:c.805G>C

ENST00000455727.6:c.314-1935G>C

ENST00000535915.5:c.428G>C

ENST00000545707.5:c.314-1108G>C

ENST00000557933.5:c.551G>C

ENST00000558013.5:c.551G>C

ENST00000558518.5:c.551G>C

ENST00000560467.1:c.151G>C

NM_000527.4:c.551G>C

NM_001195798.1:c.551G>C

NM_001195799.1:c.428G>C

NM_001195800.1:c.314-1935G>C

NM_001195803.1:c.314-1108G>C

NM_001195798.2:c.551G>C

NM_001195799.2:c.428G>C

NM_001195800.2:c.314-1935G>C

NM_001195803.2:c.314-1108G>C

Likely Pathogenic

Met criteria codes **4**

PP3 PP4 PM2 PM1

Not Met criteria codes **17**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

BP7

BP4

BP2

PS1

PS2

PS3

PS4

PP1

PM6

PM3

PM5

PM4

PVS1

BA1

BS1

BS4

BS3

Evidence Links 0

- [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.551G>C (p.Cys184Ser) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM1, PM2, PP3, 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: PM1 - Variant meets PM2 and alters Cys184, one of the cysteine residues listed. PM2 - This variant is absent from gnomAD (gnomAD v2.1.1). PP3 - REVEL = 0.871. It is above 0.75. PP4 - Variant meets PM2 and is identified in 1 index case who fulfills DLCN>=6 criteria for FH from Service de Biochimie et de Biologie Moléculaire, Hospices Civils de Lyon, Lyon, France, after alternative causes for high cholesterol were excluded.

Met criteria codes

PP3			REVEL = 0.871. It is above 0.75, so PP3 is Met.
PP4			Variant meets PM2 and is identified in 1 index case who fulfills DLCN>=6 criteria for FH from Service de Biochimie et de Biologie Moléculaire, Hospices Civils de Lyon, Lyon, France, so PP4 is Met.
PM2			This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is Met.
PM1			Variant meets PM2 and alters Cys184, one of the cysteine residues listed, so PM1 is Met.

Not Met criteria codes

BP7			Variant is not synonymous, so BP7 is Not Met.
BP4			REVEL = 0.871. It is not below 0.50, so BP4 is Not Met.
BP2			Not observed in trans with other LP/P variants, so BP2 is Not Met.
PS1			Variant meets PM1 (alters Cys184, one of the cysteine residues listed), so PS1 is not met.
PS2			de novo occurrence data not reported, so PS2 is Not Met.
PS3			There are no functional studies reported for this variant, so PS3 is not met.

