

Variant: *NM_000527.5(LDLR):c.2041T>G (p.Cys681Gly)*

Version: 1.0

CA10585740 [↗](#)

252185 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 6ea22d66-0335-4bd2-9889-74e670390de4

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HGVS expressions

NM_000527.5(LDLR):c.2041T>G (p.Cys681Gly)

NM_000527.5:c.2041T>G

NC_000019.10:g.11120423T>G

CM000681.2:g.11120423T>G

NC_000019.9:g.11231099T>G

CM000681.1:g.11231099T>G

NC_000019.8:g.11092099T>G

NG_009060.1:g.36043T>G

ENST00000252444.10:c.2299T>G

ENST00000559340.2:c.*110T>G

ENST00000560467.2:c.1921T>G

ENST00000558518.6:c.2041T>G

ENST00000252444.9:c.2295T>G

ENST00000455727.6:c.1537T>G

ENST00000535915.5:c.1918T>G

ENST00000545707.5:c.1606+190T>G

ENST00000557933.5:c.2041T>G

ENST00000558013.5:c.2041T>G

ENST00000558518.5:c.2041T>G

NM_000527.4:c.2041T>G

NM_001195798.1:c.2041T>G

NM_001195799.1:c.1918T>G

NM_001195800.1:c.1537T>G

NM_001195803.1:c.1606+190T>G

NM_001195798.2:c.2041T>G

NM_001195799.2:c.1918T>G

NM_001195800.2:c.1537T>G

NM_001195803.2:c.1606+190T>G

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM2 PM1

Not Met criteria codes 5

BS1 BP4 PS1 BA1 PM5

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.2041T>G (p.Cys681Gly) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM1, PM2, PP3 and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 24 March 2025. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v.4.1.0). PM1: Variant meets PM2 and alters Cys681, one of the cysteine residues listed. PP3: REVEL = 0.957. PP4: Variant meets PM2 and is identified in 1 case with DLCN score >=6 in PMID 18648394 (Snozek et al., 2009), after alternative causes of high cholesterol were excluded.

Met criteria codes

PP3			REVEL = 0.957, above 0.75
PP4			Variant meets PM2. Identified in 1 FH case (PMID: 18648394) with DLCN ≥ 6, after alternative causes of high cholesterol were excluded. Note, variant is in cis with LDLR c.-217C>T, which has been classified as benign by the VCEP.
PM2			This variant is absent from gnomAD (gnomAD v4.1.0)
PM1			Variant meets PM2 and alters Cys681, one of the cysteine residues listed.

Not Met criteria codes

BS1			This variant is absent from gnomAD (gnomAD v4.1.0)
BP4			REVEL = 0.957, above 0.75
PS1			Variant meets PM1 and 1 other missense variants in the same codon: - NM_000527.5(LDLR):c.2041T>A (p.Cys681Ser) (ClinVar ID 252184) - Conflicting evidence of pathogenicity by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.
BA1			This variant is absent from gnomAD (gnomAD v4.1.0)
PM5			Variant meets PM1 and 1 other missense variants in the same codon: - NM_000527.5(LDLR):c.2041T>A (p.Cys681Ser) (ClinVar ID 252184) - Conflicting evidence of pathogenicity by these guidelines There is no variant in

the same codon classified as Pathogenic by these guidelines.

Curation History



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The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.