

Variant: NM_000527.5(LDLR):c.905G>A (p.Cys302Tyr)

Version: 1.0

CA10585186 [↗](#)

251515 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 686d8d2d-402e-40b6-aa64-cb4121c3575d

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HGVS expressions

NM_000527.5(LDLR):c.905G>A (p.Cys302Tyr)

NM_000527.5:c.905G>A

NC_000019.10:g.11107479G>A

CM000681.2:g.11107479G>A

NC_000019.9:g.11218155G>A

CM000681.1:g.11218155G>A

NC_000019.8:g.11079155G>A

NG_009060.1:g.23099G>A

ENST00000252444.10:c.1163G>A

ENST00000559340.2:c.905G>A

ENST00000560467.2:c.905G>A

ENST00000558518.6:c.905G>A

ENST00000252444.9:c.1159G>A

ENST00000455727.6:c.401G>A

ENST00000535915.5:c.782G>A

ENST00000545707.5:c.524G>A

ENST00000557933.5:c.905G>A

ENST00000558013.5:c.905G>A

ENST00000558518.5:c.905G>A

ENST00000558528.1:n.420G>A

ENST00000560467.1:c.505G>A

NM_000527.4:c.905G>A

NM_001195798.1:c.905G>A

NM_001195799.1:c.782G>A

NM_001195800.1:c.401G>A

NM_001195803.1:c.524G>A

NM_001195798.2:c.905G>A

NM_001195799.2:c.782G>A

NM_001195800.2:c.401G>A

NM_001195803.2:c.524G>A

Likely Pathogenic

Met criteria codes 5

PP3PP4PM2PM1PS4_Supporting

Not Met criteria codes 17

BP7BP4BP2PS1PS2PS3PP1PM6PM3PM5PM4PVS1BA1BS2BS1BS4BS3

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			
<p>The NM_000527.5(LDLR):c.905G>A (p.Cys302Tyr) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM1, PM2, PP3, PP4 and PS4_Supporting as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 23 June 2023. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD version 2.1.1). PP3: REVEL= 0.98. PM1: Variant meets PM2 and alters Cys302, one of the cysteine residues listed. PS4_Supporting, PP4: Variant meets PM2 and is identified in 2 index cases who fulfill criteria for FH (Japan Atherosclerosis Society) from PMID 33461934 (Tada et al., 2021), after alternative causes of high cholesterol were excluded.</p>			
Met criteria codes			
PP3			REVEL= 0.98, this is greater than 0.75.
PP4			Variant meets PM2 and is identified in at least 1 index case who fulfills Japan Atherosclerosis Society criteria for FH from PMID 33461934, after alternative causes of high cholesterol were excluded.
PM2			This variant is absent from gnomAD (gnomAD version 2.1.1)
PM1			Variant meets PM2 and alters Cys302, one of the cysteine residues listed.
PS4_Supporting			Variant meets PM2 and is identified in 2 index cases who fulfill Japan Atherosclerosis Society criteria for FH from PMID 33461934, after alternative causes of high cholesterol were excluded.
Not Met criteria codes			
BP7			Not a synonymous variant.
BP4			REVEL = 0.98, this is greater than 0.50.
BP2			No data.

PS1			Variant meets criteria for PM1.
PS2			Not met.
PS3			No data.
PP1			No data.
PM6			Not met.
PM3			No data.
PM5			Variant meets criteria for PM1.
PM4			Not an in-frame deletion/insertion.
PVS1			Not a null variant.
BA1			This variant is absent from gnomAD (gnomAD version 2.1.1)
BS2			No data.
BS1			This variant is absent from gnomAD (gnomAD version 2.1.1)
BS4			No data.
BS3			No data.

Curation History 		
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