

Variant: NM_000527.5(LDLR):c.1028G>T (p.Gly343Val)

Version: 1.0

CA404082758 [↗](#)

440618 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 489ea19a-f7c7-446d-ade9-aae9ee6160ed

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HGVS expressions

NM_000527.5:c.1028G>T

NM_000527.5(LDLR):c.1028G>T (p.Gly343Val)

NC_000019.10:g.11110739G>T

CM000681.2:g.11110739G>T

NC_000019.9:g.11221415G>T

CM000681.1:g.11221415G>T

NC_000019.8:g.11082415G>T

NG_009060.1:g.26359G>T

ENST00000252444.10:c.1286G>T

ENST00000559340.2:c.1028G>T

ENST00000560467.2:c.941-775G>T

ENST00000558518.6:c.1028G>T

ENST00000252444.9:c.1282G>T

ENST00000455727.6:c.524G>T

ENST00000535915.5:c.905G>T

ENST00000545707.5:c.647G>T

ENST00000557933.5:c.1028G>T

ENST00000558013.5:c.1028G>T

ENST00000558518.5:c.1028G>T

ENST00000560173.1:n.27G>T

ENST00000560467.1:c.541-775G>T

NM_000527.4:c.1028G>T

NM_001195798.1:c.1028G>T

NM_001195799.1:c.905G>T

NM_001195800.1:c.524G>T

NM_001195803.1:c.647G>T

NM_001195798.2:c.1028G>T

NM_001195799.2:c.905G>T

NM_001195800.2:c.524G>T

NM_001195803.2:c.647G>T

Likely Pathogenic

Met criteria codes 3

PP3PM5_StrongPM2

Not Met criteria codes 3

PS3PS4PP4

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.1028G>T (p.Gly343Val) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM2, PP3, PM5_Strong) 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 is absent from gnomAD (gnomAD v2.1.1). PP3: REVEL=0.983, it is above 0.75. PM5_Strong: Three other variants at the same codon: NM_000527.5(LDLR):c.1028G>A (p.Gly343Asp)(ClinVarID 251606) is classified as Likely Pathogenic, NM_000527.5(LDLR):c.1027G>T (p.Gly343Cys)(ClinVarID 251605) is classified as Pathogenic, NM_000527.5(LDLR):c.1027G>A (p.Gly343Ser)(ClinVarID 183106) is classified as Pathogenic by these guidelines, therefore PM5_Strong is met. PP4, PS4 not met: Variant meets PM2, and is reported in 1 index case, but the FH diagnosis and clinical information for the patient is not clear, reported by Miyake et al, 2009, National Cardiovascular Center Research Institute, Osaka, Japan, PMID18718593. PS3 not met: Functional data is not available.

Met criteria codes

PP3	i	✓	PP3: REVEL=0.983, it is above 0.75.
PM5_Strong	i	✓	Three other variants at the same codon: NM_000527.5(LDLR):c.1028G>A (p.Gly343Asp)(ClinVarID 251606) is classified as Likely Pathogenic, NM_000527.5(LDLR):c.1027G>T (p.Gly343Cys)(ClinVarID 251605) is classified as Pathogenic, NM_000527.5(LDLR):c.1027G>A (p.Gly343Ser)(ClinVarID 183106) is classified as Pathogenic by these guidelines, therefore PM5_Strong is met.
PM2	i	✓	This variant is absent from gnomAD (gnomAD v2.1.1).

Not Met criteria codes

PS3	i	✗	Functional data is not available.
PS4	i	✗	Variant meets PM2, and is reported in 1 index case, but the FH diagnosis and clinical information for the patient is not clear, reported by Miyake et al, 2009, National Cardiovascular Center Research Institute, Osaka, Japan, PMID18718593.
PP4	i	✗	

Variant meets PM2, and is reported in 1 index case, but the FH diagnosis and clinical information for the patient is not clear, reported by Miyake et al, 2009, National Cardiovascular Center Research Institute, Osaka, Japan, PMID18718593.

Curation History [↗](#)

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Showing 1 to 1 of 1 rows

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