The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2023/4/28
Published on: 2023/5/1

HGVS expressions

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

PM2 PP3 PM5_Strong

Not Met criteria codes 3

PS3 PS4 PP4

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

PM2	✔	This variant is absent from gnomAD (gnomAD v2.1.1).
PP3	✔	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.

Not Met criteria codes

PS3	✖	Functional data is not available.
PS4	✖	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	✖	

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

nowing 1 to 1 of 1 rows

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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.