

Variant: NM_000527.5(LDLR):c.845T>G (p.Phe282Cys)

Version: 1.0

CA404080624 [↗](#)

977997 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 8ec9b766-260e-4587-8f2c-cec8efefbe1f

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HGVS expressions

NM_000527.5:c.845T>G

NM_000527.5(LDLR):c.845T>G (p.Phe282Cys)

NC_000019.10:g.11107419T>G

CM000681.2:g.11107419T>G

NC_000019.9:g.11218095T>G

CM000681.1:g.11218095T>G

NC_000019.8:g.11079095T>G

NG_009060.1:g.23039T>G

ENST00000252444.10:c.1103T>G

ENST00000559340.2:c.845T>G

ENST00000560467.2:c.845T>G

ENST00000558518.6:c.845T>G

ENST00000252444.9:c.1099T>G

ENST00000455727.6:c.341T>G

ENST00000535915.5:c.722T>G

ENST00000545707.5:c.464T>G

ENST00000557933.5:c.845T>G

ENST00000558013.5:c.845T>G

ENST00000558518.5:c.845T>G

ENST00000558528.1:n.360T>G

ENST00000560467.1:c.445T>G

NM_000527.4:c.845T>G

NM_001195798.1:c.845T>G

NM_001195799.1:c.722T>G

NM_001195800.1:c.341T>G

NM_001195803.1:c.464T>G

NM_001195798.2:c.845T>G

NM_001195799.2:c.722T>G

NM_001195800.2:c.341T>G

NM_001195803.2:c.464T>G

Uncertain Significance

Met criteria codes2

PP3PM2

Not Met criteria codes20

BA1BS2BS1BS4BS3BP4BP3BP2PVS1PS1PS2PS3PS4PP1PP4PM1PM3PM5PM4PM6

Evidence Links0

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.845T>G (p.Phe282Cys) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes PM2 and PP3 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). So, PM2 is met. PP3: REVEL=0.975. It is above 0.75, so PP3 is met.

Met criteria codes

PP3			REVEL=0.975. It is above 0.75, so PP3 is met.
PM2			This variant is absent from gnomAD (gnomAD v2.1.1). So, PM2 is met.

Not Met criteria codes

BA1			This variant is absent from gnomAD (gnomAD v2.1.1).
BS2			No data available
BS1			This variant is absent from gnomAD (gnomAD v2.1.1).
BS4			No data available
BS3			No data available
BP4			REVEL=0.975. It is above 0.5
BP3			No in-frame deletions/insertions

BP2			No data available
PVS1			Not a null variant.
PS1			No other missense variant in this codon with the same amino acid change.
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No data available
PS4			No data available
PP1			No data available
PP4			No data available
PM1			Not in exon 4. Not a cysteine residue.
PM3			No data available
PM5			4 other missense variants in the same codon: - NM_000527.5(LDLR):c.845T>A (p.Phe282Tyr) (ClinVar ID 1763461) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.845T>C (p.Phe282Ser) (ClinVar ID 1466547) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.844T>C (p.Phe282Leu) (ClinVar ID 977996) - classified as uncertain significance by these guidelines - NM_000527.5(LDLR):c.846C>A (p.Phe282Leu) (ClinVar ID 183098) - classified as Likely pathogenic by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.
PM4			No in-frame deletions/insertions
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 

Showing 1 to 1 of 1 rows

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