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.826T>C (p.Cys276Arg)

Version: 1.0

CA10585154

251479 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: cd4e74cd-7511-489e-8c09-823f567a973d
Approved on: 2022/10/28
Published on: 2024/12/9

HGVS expressions

NM_000527.5:c.826T>C
NM_000527.5(LDLR):c.826T>C (p.Cys276Arg)
NC_000019.10:g.11107400T>C
CM000681.2:g.11107400T>C
NC_000019.9:g.11218076T>C
CM000681.1:g.11218076T>C
NC_000019.8:g.11079076T>C
NG_009060.1:g.23020T>C
ENST00000252444.10:c.1084T>C
ENST00000559340.2:c.826T>C
ENST00000560467.2:c.826T>C
ENST00000558518.6:c.826T>C
ENST00000252444.9:c.1080T>C
ENST00000455727.6:c.322T>C
ENST00000535915.5:c.703T>C
ENST00000545707.5:c.445T>C
ENST00000557933.5:c.826T>C
ENST00000558013.5:c.826T>C
ENST00000558518.5:c.826T>C
ENST00000558528.1:n.341T>C
ENST00000560467.1:c.426T>C
NM_000527.4:c.826T>C
NM_001195798.1:c.826T>C
NM_001195799.1:c.703T>C
NM_001195800.1:c.322T>C
NM_001195803.1:c.445T>C
NM_001195798.2:c.826T>C
NM_001195799.2:c.703T>C
NM_001195800.2:c.322T>C
NM_001195803.2:c.445T>C

Likely Pathogenic

Met criteria codes 5

PM1 PM2 PS4_Supporting PP3 PP4

Not Met criteria codes 21

PM3 PM5 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP5 BP7 BP4 BP3 BP1 BP2 PVS1 PS1 PS2 PS3 PP1 PP2

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.826T>C (p.Cys276Arg) 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 28 October 2022. The supporting evidence is as follows: PM1: Variant meets PM2 and alters Cys276. PM2: This variant is absent from gnomAD v2.1.1. PP3: REVEL = 0.915. PS4_Supporting, PP4: Variant meets PM2 and is identified in at least 3 unrelated index cases who fulfill criteria for FH (3 cases from PMID 10978268 (Bertolini et al. 2000)).

Met criteria codes

PM1	✔	Variant meets PM2 and is missense in exon 4/alters Cys276.
PM2	✔	This variant is absent from gnomAD v2.1.1
PS4_Supporting	✔	Variant meets PM2 and is identified in at least 2 unrelated index cases who fulfill SB criteria for FH from PMID 23375686 and 10978268.
PP3	✔	REVEL = 0.915
PP4	✔	Variant meets PM2 and is identified in at least 1 index case who fulfills SB possible criteria for FH from PMID 23375686, after alternative causes of high cholesterol were excluded.

Not Met criteria codes

PM3	✖	Not met.
PM5	✖	Not met.
PM4	✖	Not an in-frame deletion or insertion.

PM6		✖	Not met.
BA1		✖	Not met.
BS2		✖	Not identified in normolipidemic individuals
BS1		✖	Not met.
BS4		✖	Not met.
BS3		✖	No functional data.
BP5		✖	Not applicable
BP7		✖	Not a synonymous variant.
BP4		✖	REVEL = 0.915
BP3		✖	Not applicable
BP1		✖	Not applicable
BP2		✖	Not met.
PVS1		✖	Not a null variant.
PS1		✖	Not met.
PS2		✖	Not met.
PS3		✖	No functional data.
PP1		✖	Not met.
PP2		✖	Not applicable

Curation History

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