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.2546C>A (p.Ser849Ter)

Version: 1.0

CA10585878

252350 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 0c970ab1-3278-4f04-af3a-5b8859e99901
Approved on: 2021/6/22
Published on: 2021/6/24

HGVS expressions

NM_000527.5(LDLR):c.2546C>A (p.Ser849Ter)
NM_000527.5:c.2546C>A
NC_000019.10:g.11129669C>A
CM000681.2:g.11129669C>A
NC_000019.9:g.11240345C>A
CM000681.1:g.11240345C>A
NC_000019.8:g.11101345C>A
NG_009060.1:g.45289C>A
ENST00000252444.10:c.2804C>A
ENST00000559340.2:c.*615C>A
ENST00000560467.2:c.2426C>A
ENST00000558518.6:c.2546C>A
ENST00000252444.9:c.2800C>A
ENST00000455727.6:c.2042C>A
ENST00000535915.5:c.2423C>A
ENST00000545707.5:c.2012C>A
ENST00000557933.5:c.2608C>A
ENST00000558013.5:c.2546C>A
ENST00000558518.5:c.2546C>A
ENST00000560628.1:n.108+2015C>A
NM_000527.4:c.2546C>A
NM_001195798.1:c.2546C>A
NM_001195799.1:c.2423C>A
NM_001195800.1:c.2042C>A
NM_001195803.1:c.2012C>A
NM_001195798.2:c.2546C>A
NM_001195799.2:c.2423C>A
NM_001195800.2:c.2042C>A
NM_001195803.2:c.2012C>A

Likely Pathogenic

Met criteria codes 4

PP4 PM2 PS4_Supporting PVS1_Moderate

Not Met criteria codes 22

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

PP1 PP2 PP3 BA1 PM1
PM3 PM5 PM4 PM6 BS2
BS1 BS4 BS3 PS1 PS2 PS3
BP5 BP7 BP4 BP3 BP1 BP2

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.2546C>A (p.Ser849Ter) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM2, PVS1_Moderate, PP4 and PS4_Supporting) as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (https://doi.org/10.1101/2021.03.17.21252755). The supporting evidence is as follows: PM2 - No population data was found for this allele in gnomAD (gnomAD v2.1.1). PVS1_moderate - Variant is nonsense after amino acid 830 (NM_000527.5:p.Lys830). PP4 - Variant meets PM2. Variant identified in 2 index FH cases (1 case from Color laboratory with Simon-Broome criteria; 1 case with Simon-Broome criteria published in PMID: 26892515). PS4_supporting - Variant meets PM2. Variant identified in 2 index cases (1 case from Color laboratory with Simon-Broome criteria; 1 case with Simon-Broome criteria published in PMID: 26892515).

Met criteria codes

PP4	✔	Variant meets PM2. Variant identified in 2 index FH cases (1 case from Color laboratory with Simon-Broome criteria; 1 case with Simon-Broome criteria published in PMID: 26892515).
PM2	✔	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
PS4_Supporting	✔	Variant meets PM2. Variant identified in 2 index cases (1 case from Color laboratory with Simon-Broome criteria; 1 case with Simon-Broome criteria published in PMID: 26892515).
PVS1_Moderate	✔	Variant is nonsense after amino acid 830 (NM_000527.5:p.Lys830).

Not Met criteria codes

PP1	✖	Family members not tested.
PP2	✖	Not applicable.
PP3	✖	Nonsense variant that meets PVS1. Not applicable.
BA1	✖	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
PM1	✖	Nonsense variant. Not applicable.

PM3		✖	Not identified in individuals with other variants.
PM5		✖	Nonsense variant. Not applicable.
PM4		✖	Nonsense variant. Not applicable.
PM6		✖	No de novo cases were identified.
BS2		✖	No unaffected individuals identified with the variant.
BS1		✖	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
BS4		✖	Family members not tested.
BS3		✖	No functional assays performed/found - not applicable.
PS1		✖	Nonsense variant. Not applicable.
PS2		✖	No de novo cases were identified.
PS3		✖	No functional assays performed/found - not applicable.
BP5		✖	Not applicable
BP7		✖	Nonsense variant. Not applicable.
BP4		✖	Nonsense variant that meets PVS1. Not applicable.
BP3		✖	Not applicable.
BP1		✖	Not applicable.
BP2		✖	Not identified in individuals with other variants.

Curation History

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