

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

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HGVS expressions

NM_000527.5:c.2546C>A

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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**

PVS1_Moderate

PP4

PM2

PS4_Supporting

Not Met criteria codes **22**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

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

[Criteria Specifications for this VCEP](#)

Evidence Links 0

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

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).
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).

Not Met criteria codes

BA1			No population data was found for this allele in gnomAD (gnomAD v2.1.1).
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.
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.
BS2			No unaffected individuals identified with the variant.
PP1			Family members not tested.
PP2			Not applicable.
PP3			Nonsense variant that meets PVS1. Not applicable.
PM6			No de novo cases were identified.
PM1			Nonsense variant. Not applicable.
PM3			Not identified in individuals with other variants.
PM5			Nonsense variant. Not applicable.
PM4			Nonsense variant. Not applicable.
PS1			Nonsense variant. Not applicable.
PS2			No de novo cases were identified.
PS3			No functional assays performed/found - not applicable.

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