

Variant: NM_000527.5(LDLR):c.1457G>A (p.Ser486Asn)

Version: 1.0

CA10585463 [↗](#)

251853 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: ec4c063a-9ce4-414d-b634-eb143213bb92

Approved on: 2024/10/28

Published on: 2025/1/19

HGVS expressions

NM_000527.5(LDLR):c.1457G>A (p.Ser486Asn)

NM_000527.5:c.1457G>A

NC_000019.10:g.11113633G>A

CM000681.2:g.11113633G>A

NC_000019.9:g.11224309G>A

CM000681.1:g.11224309G>A

NC_000019.8:g.11085309G>A

NG_009060.1:g.29253G>A

ENST00000252444.10:c.1715G>A

ENST00000559340.2:c.1457G>A

ENST00000560467.2:c.1337G>A

ENST00000558518.6:c.1457G>A

ENST00000252444.9:c.1711G>A

ENST00000455727.6:c.953G>A

ENST00000535915.5:c.1334G>A

ENST00000545707.5:c.1076G>A

ENST00000557933.5:c.1457G>A

ENST00000558013.5:c.1457G>A

ENST00000558518.5:c.1457G>A

ENST00000559340.1:c.178G>A

NM_000527.4:c.1457G>A

NM_001195798.1:c.1457G>A

NM_001195799.1:c.1334G>A

NM_001195800.1:c.953G>A

NM_001195803.1:c.1076G>A

NM_001195798.2:c.1457G>A

NM_001195799.2:c.1334G>A

NM_001195800.2:c.953G>A

NM_001195803.2:c.1076G>A

Uncertain Significance

Met criteria codes **2**

PM2 BP4

Not Met criteria codes **6**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1457G>A (p.Ser486Asn) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2 and BP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 28 October 2024. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v4.1.0). BP4: REVEL = 0.297. It is below 0.5, splicing evaluation needed. Functional data on splicing not available. A) Not on limits B) Does not create a DeNovo AG or GT C) There is no GT or AG nearby. Variant is not predicted to alter splicing.

Met criteria codes

PM2	i	✓	This variant is absent from gnomAD (gnomAD v4.1.0)
BP4	i	✓	REVEL = 0.297. It is not above 0.75, splicing evaluation needed. Functional data on splicing not available. A) Not on limits B) Does not create a DeNovo AG or GT C) There is no GT or AG nearby Variant is not predicted to alter splicing.

Not Met criteria codes

PS1	i	✗	There are no variants causing the same amino acid change classified as Pathogenic by these guidelines.
BA1	i	✗	This variant is absent from gnomAD (gnomAD v4.1.0)
PP3	i	✗	REVEL = 0.297. It is not above 0.75, splicing evaluation needed. Functional data on splicing not available. A) Not on limits B) Does not create a DeNovo AG or GT C) There is no GT or AG nearby Variant is not predicted to alter splicing.
PP4	i	✗	No cases identified.
PM5	i	✗	1 other missense variant in the same codon: - NM_000527.5(LDLR):c.1456A>G (p.Ser486Gly) (ClinVar ID 251852) - VUS by these guidelines There are no variants in the same codon classified as Pathogenic by these guidelines.
BS1	i	✗	This variant is absent from gnomAD (gnomAD v4.1.0)

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