

Variant: *NM_000527.5(LDLR):c.797A>G (p.Asp266Gly)*

Version: 1.0

CA10585136 [↗](#)

251457 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: d5c3419c-4f00-4eaa-b2e3-fba4693b3851

Approved on: 2021/11/14

Published on: 2022/6/30

HGVS expressions

NM_000527.5(LDLR):c.797A>G (p.Asp266Gly)

NM_000527.5:c.797A>G

NC_000019.10:g.11106667A>G

CM000681.2:g.11106667A>G

NC_000019.9:g.11217343A>G

CM000681.1:g.11217343A>G

NC_000019.8:g.11078343A>G

NG_009060.1:g.22287A>G

ENST00000252444.10:c.1055A>G

ENST00000559340.2:c.797A>G

ENST00000560467.2:c.797A>G

ENST00000558518.6:c.797A>G

ENST00000252444.9:c.1051A>G

ENST00000455727.6:c.314-725A>G

ENST00000535915.5:c.674A>G

ENST00000545707.5:c.416A>G

ENST00000557933.5:c.797A>G

ENST00000558013.5:c.797A>G

ENST00000558518.5:c.797A>G

ENST00000558528.1:n.312A>G

ENST00000560467.1:c.397A>G

NM_000527.4:c.797A>G

NM_001195798.1:c.797A>G

NM_001195799.1:c.674A>G

NM_001195800.1:c.314-725A>G

NM_001195803.1:c.416A>G

NM_001195798.2:c.797A>G

NM_001195799.2:c.674A>G

NM_001195800.2:c.314-725A>G

NM_001195803.2:c.416A>G

Likely Pathogenic

Met criteria codes **5**

PS4_Supporting

PM5_Strong

PP3

PP4

PM2

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

Not Met criteria codes 21

BA1 BP5 BP7 BP4 BP3 BP1
BP2 BS2 BS1 BS4 BS3 PP1
PP2 PM1 PM3 PM4 PM6
PVS1 PS1 PS2 PS3

Evidence Links 0

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR): c.797A>G (p.Asp266Gly) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes PM5_Strong, PM2, PP3, 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>). PM5_Strong - 4 other missense variants in the same codon: - NM_000527.5(LDLR): c.796G>T (p.Asp266Asn) (ClinVar ID 226334) - Pathogenic by these guidelines, - NM_000527.5(LDLR): c.797A>T (p.Asp266Val) (ClinVar ID 251458) - Likely pathogenic by these guidelines, - NM_000527.5(LDLR): c.796A>T (p.Asp266Tyr) (ClinVar ID 251456) - Pathogenic by these guidelines, - NM_000527.5(LDLR):c.798T>A (p.Asp266Glu) - (ClinVar ID 161287) - Pathogenic by these guidelines. There are 3 variants in the same codon classified as Pathogenic by these guidelines; PM2 - This variant is absent from gnomAD (gnomAD v2.1.1); PP3 - REVEL = 0.98; PP4 - Identified in 2 unrelated index cases fulfilling Simon-Broome criteria (published in PMID: 32331935); PS4_Supporting - Variant meets PM2. Identified in 2 unrelated index cases fulfilling Simon-Broome criteria (published in PMID: 32331935);

Met criteria codes

PS4_Supporting			Variant meets PM2. Identified in 2 unrelated index cases fulfilling Simon-Broome criteria (published in PMID: 32331935)
PM5_Strong			4 other missense variants in the same codon: - NM_000527.5(LDLR): c.796G>T (p.Asp266Asn) (ClinVar ID 226334) - Pathogenic by these guidelines, - NM_000527.5(LDLR): c.797A>T (p.Asp266Val) (ClinVar ID 251458) - Likely pathogenic by these guidelines, - NM_000527.5(LDLR): c.796A>T (p.Asp266Tyr) (ClinVar ID 251456) - Pathogenic by these guidelines, - NM_000527.5(LDLR):c.798T>A (p.Asp266Glu) - (ClinVar ID 161287) - Pathogenic by these guidelines. There are 3 variants in the same codon classified as Pathogenic by these guidelines;
PP3			REVEL = 0.98
PP4			Identified in 2 unrelated index cases fulfilling Simon-Broome criteria (published in PMID: 32331935)
PM2			This variant is absent from gnomAD (gnomAD v2.1.1).

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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