

Variant: *NM_000527.5(LDLR):c.2531G>A (p.Gly844Asp)*

Version: 1.0

CA023681 [↗](#)

3734 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 58ad8eee-de96-4112-af59-af6615224440

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HGVS expressions

NM_000527.5(LDLR):c.2531G>A (p.Gly844Asp)

NM_000527.5:c.2531G>A

NC_000019.10:g.11129654G>A

CM000681.2:g.11129654G>A

NC_000019.9:g.11240330G>A

CM000681.1:g.11240330G>A

NC_000019.8:g.11101330G>A

NG_009060.1:g.45274G>A

ENST00000252444.10:c.2789G>A

ENST00000559340.2:c.*600G>A

ENST00000560467.2:c.2411G>A

ENST00000558518.6:c.2531G>A

ENST00000252444.9:c.2785G>A

ENST00000455727.6:c.2027G>A

ENST00000535915.5:c.2408G>A

ENST00000545707.5:c.1997G>A

ENST00000557933.5:c.2593G>A

ENST00000558013.5:c.2531G>A

ENST00000558518.5:c.2531G>A

ENST00000560628.1:n.108+2000G>A

NM_000527.4:c.2531G>A

NM_001195798.1:c.2531G>A

NM_001195799.1:c.2408G>A

NM_001195800.1:c.2027G>A

NM_001195803.1:c.1997G>A

NM_001195798.2:c.2531G>A

NM_001195799.2:c.2408G>A

NM_001195800.2:c.2027G>A

NM_001195803.2:c.1997G>A

Likely Pathogenic

Met criteria codes **4**

PS4 PP3 PP4 PM2

Not Met criteria codes **22**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

BS2	BS1	BS4	BS3	BP4	BP3
BP1	BP2	PVS1	BP5	BP7	
BA1	PS1	PS2	PS3	PP1	PP2
PM6	PM1	PM3	PM5	PM4	

[Criteria Specifications for this VCEP](#)

Evidence Links 1

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.2531G>A (p.Gly844Asp) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PS4, PM2, PP3 and PP4) 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: PS4 - Variant meets PM2 and is identified in 14 unrelated index cases fulfilling Simon-Broome criteria published in PMID: 7573037. PM2 - No population data was found for this variant in gnomAD (gnomAD v2.1.1). PP3 - REVEL: 0,939. PP4 - Variant meets PM2 and is identified in 14 unrelated index cases fulfilling Simon-Broome criteria for FH published in PMID: 7573037.

Met criteria codes

PS4		✓	Variant meets PM2 and is identified in 14 unrelated index cases fulfilling Simon-Broome criteria published in PMID: 7573037.
PP3		✓	REVEL: 0,939. Score is above 0,75.
PP4		✓	Variant meets PM2 and is identified in 14 unrelated index cases fulfilling Simon-Broome criteria for FH published in PMID: 7573037.
PM2		✓	No population data was found for this variant in gnomAD (gnomAD v2.1.1).

Not Met criteria codes

BS2		✗	No unaffected individuals identified with the variant.
BS1		✗	No population data was found for this variant in gnomAD (gnomAD v2.1.1).
BS4		✗	No family members tested.
BS3		✗	BS3 not met. PMID: 11389828 - defect in polarized targeting of the receptor in hepatocytes. defect in polarized targeting of the receptor in hepatocytes PubMed:11389828
BP4		✗	REVEL: 0,939. Score is not below 0,50.

BP3			Not applicable.
BP1			Not applicable.
BP2			Not identified in individuals with other variants.
PVS1			Missense variant. Not applicable.
BP5			Not applicable.
BP7			Missense variant. Not applicable.
BA1			No population data was found for this variant in gnomAD (gnomAD v2.1.1).
PS1			No other missense variants leads to the same amino acid change.
PS2			No de novo cases were identified.
PS3			PS3 not met. PMID: 11389828 - defect in polarized targeting of the receptor in hepatocytes. defect in polarized targeting of the receptor in hepatocytes PubMed:11389828 
PP1			No family members tested.
PP2			Not applicable.
PM6			No de novo cases were identified.
PM1			Missense at codon 844 - it is not exon 4 or any of the 60 Cys residues listed. Not applicable.
PM3			Not identified in individuals with other variants.
PM5			One other missense variant in the same codon: (1)NM_000527.4(LDLR):c.2530G>A (p.Gly844Ser) (ClinVar ID 440701) - VUS by these guidelines No other missense variants in the same codon classified as Pathogenic.
PM4			Missense variant. Not applicable.

Showing 1 to 1 of 1 rows

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