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.1080T>G (p.Asp360Glu)

Version: 1.0

CA031958

440624 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 11a66486-f4d3-4363-ab30-6cf80fcc7826
Approved on: 2024/10/28
Published on: 2025/1/19

HGVS expressions

NM_000527.5:c.1080T>G
NM_000527.5(LDLR):c.1080T>G (p.Asp360Glu)
NC_000019.10:g.11111533T>G
CM000681.2:g.11111533T>G
NC_000019.9:g.11222209T>G
CM000681.1:g.11222209T>G
NC_000019.8:g.11083209T>G
NG_009060.1:g.27153T>G
ENST00000252444.10:c.1338T>G
ENST00000559340.2:c.1080T>G
ENST00000560467.2:c.960T>G
ENST00000558518.6:c.1080T>G
ENST00000252444.9:c.1334T>G
ENST00000455727.6:c.576T>G
ENST00000535915.5:c.957T>G
ENST00000545707.5:c.699T>G
ENST00000557933.5:c.1080T>G
ENST00000558013.5:c.1080T>G
ENST00000558518.5:c.1080T>G
ENST00000560173.1:n.79T>G
ENST00000560467.1:c.560T>G
NM_000527.4:c.1080T>G
NM_001195798.1:c.1080T>G
NM_001195799.1:c.957T>G
NM_001195800.1:c.576T>G
NM_001195803.1:c.699T>G
NM_001195798.2:c.1080T>G
NM_001195799.2:c.957T>G
NM_001195800.2:c.576T>G
NM_001195803.2:c.699T>G

Uncertain Significance

Met criteria codes 1

BP4

Not Met criteria codes 9

BS1 BP2 PS1 PS4 PM5 PM2 PP3 PP4 BA1

Evidence Links 0

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Familial Hypercholesterolemia Expert Panel Specifications to the ACMG/AMP Variant Classification Guidelines Version 1.2*
  - **PDF**
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1080T>G (p.Asp360Glu) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence code 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: BP4: REVEL = 0.404. it is below 0.50, so splicing evaluation is required. Functional data on splicing not available. A) not on limits B) it creates a de novo AG, but de novo score is below 0.8. Variant is not predicted to alter splicing.

Met criteria codes

BP4	✔	REVEL = 0.404. it is below 0.50, so splicing evaluation is required. Functional data on splicing not available. A) not on limits B) it creates a de novo AG, but de novo score is below 0.8. Variant is not predicted to alter splicing.

Not Met criteria codes

BS1	✖	FAF = 0.0001613 (0.01613%) in African/African American exomes (gnomAD v4.1.0).
BP2	✖	Could not determine whether these variants are in trans
PS1	✖	No variants causing the same amino acid change classified as Pathogenic by these guidelines.
PS4	✖	Variant found in only 1 FH case
PM5	✖	1 other missense variants in the same codon: - NM_000527.5(LDLR):c.1078G>C (p.Asp360His) (ClinVar ID 523715) - VUS by these guidelines There are no variants in the same codon classified as Pathogenic by these guidelines.
PM2	✖	PopMax MAF = 0.0002269 (0.02269%) in African/African American exomes (gnomAD v4.1.0).
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PP4		✖	Variant does not meet PM2
BA1		✖	FAF = 0.0001613 (0.01613%) in African/African American exomes (gnomAD v4.1.0).

Curation History

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