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.3G>A (p.Met1Ile)

Version: 1.0

CA404071097

440536 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 670a431d-3418-42db-9be4-6e697300ad06
Approved on: 2022/1/22
Published on: 2022/4/22

HGVS expressions

NM_000527.5(LDLR):c.3G>A (p.Met1Ile)
NM_000527.5:c.3G>A
NC_000019.10:g.11089551G>A
CM000681.2:g.11089551G>A
NC_000019.9:g.11200227G>A
CM000681.1:g.11200227G>A
NC_000019.8:g.11061227G>A
NG_009060.1:g.5171G>A
ENST00000559340.2:c.3G>A
ENST00000560467.2:c.3G>A
ENST00000558518.6:c.3G>A
ENST00000455727.6:c.3G>A
ENST00000535915.5:c.3G>A
ENST00000545707.5:c.3G>A
ENST00000557933.5:c.3G>A
ENST00000557958.1:n.89G>A
ENST00000558013.5:c.3G>A
ENST00000558518.5:c.3G>A
ENST00000560502.5:n.89G>A
NM_000527.4:c.3G>A
NM_001195798.1:c.3G>A
NM_001195799.1:c.3G>A
NM_001195800.1:c.3G>A
NM_001195803.1:c.3G>A
NM_001195798.2:c.3G>A
NM_001195799.2:c.3G>A
NM_001195800.2:c.3G>A
NM_001195803.2:c.3G>A
NR_163945.1:n.109C>T

Likely Pathogenic

Met criteria codes 3

PVS1_Moderate PM5 PM2

Not Met criteria codes 8

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

BS1 BS3 BP7 PS1 PS3 BA1 PM4 PP4

Criteria Specifications for this VCEP

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.3G>A (p.Met1Ile) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying evidence codes PM2, PVS1_Moderate, and PM5 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (https://doi.org/10.1016/j.gim.2021.09.012). The supporting evidence is as follows: PM2 - variant is absent from gnomAD (v2.1.1). PVS1_Moderate – variant is predicted to affect the initiation codon. PM5- Three other missense variants at this same codon have been reported, and one is Pathogenic: 1) NM_000527.5(LDLR):c.1A>C (p.Met1Leu) – Pathogenic by these guidelines. 2) NM_000527.5(LDLR):c.1A>G (p.Met1Val) - Likely pathogenic by these guidelines. 3) NM_000527.4(LDLR):c.2T>C (p.Met1Thr) - Likely pathogenic by these guidelines. Note: One other variant resulting in the same amino acid change at this codon has been reported: 1) NM_000527.5(LDLR):c.3G>T (p.Met1Ile) - Likely pathogenic by these guidelines. -PS1 not applicable as such variants must be Pathogenic.

Met criteria codes

PVS1_Moderate	✔	Variant is predicted to affect the initiation codon.
PM5	✔	Three other missense variants at this same codon have been reported, and one is Pathogenic: 1) NM_000527.5(LDLR):c.1A>C (p.Met1Leu) – Pathogenic by these guidelines. 2) NM_000527.5(LDLR):c.1A>G (p.Met1Val) - Likely pathogenic by these guidelines. 3) NM_000527.4(LDLR):c.2T>C (p.Met1Thr) - Likely pathogenic by these guidelines.
PM2	✔	Variant is absent from gnomAD (v2.1.1).

Not Met criteria codes

BS1	✖	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
BP7	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	Note: One other variant resulting in the same amino acid change at this codon has been reported: 1) NM_000527.5(LDLR):c.3G>T (p.Met1Ile) - Likely pathogenic by these guidelines. -PS1 not applicable as such variants must be Pathogenic.
PS3	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BA1		✖	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
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

nowing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.