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.1154T>G (p.Leu385Arg)

Version: 1.0

CA10585331

251692 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 78087d26-7297-43ed-a0d6-0688d018e704
Approved on: 2023/4/28
Published on: 2023/5/1

HGVS expressions

NM_000527.5(LDLR):c.1154T>G (p.Leu385Arg)
NM_000527.5:c.1154T>G
NC_000019.10:g.11111607T>G
CM000681.2:g.11111607T>G
NC_000019.9:g.11222283T>G
CM000681.1:g.11222283T>G
NC_000019.8:g.11083283T>G
NG_009060.1:g.27227T>G
ENST00000252444.10:c.1412T>G
ENST00000559340.2:c.1154T>G
ENST00000560467.2:c.1034T>G
ENST00000558518.6:c.1154T>G
ENST00000252444.9:c.1408T>G
ENST00000455727.6:c.650T>G
ENST00000535915.5:c.1031T>G
ENST00000545707.5:c.773T>G
ENST00000557933.5:c.1154T>G
ENST00000558013.5:c.1154T>G
ENST00000558518.5:c.1154T>G
ENST00000560173.1:n.153T>G
ENST00000560467.1:c.634T>G
NM_000527.4:c.1154T>G
NM_001195798.1:c.1154T>G
NM_001195799.1:c.1031T>G
NM_001195800.1:c.650T>G
NM_001195803.1:c.773T>G
NM_001195798.2:c.1154T>G
NM_001195799.2:c.1031T>G
NM_001195800.2:c.650T>G
NM_001195803.2:c.773T>G

Uncertain Significance

Met criteria codes 2

PM2 PP4

Not Met criteria codes 24

BS1 BS4 BS3 BS2 BP5 BP7
BP4 BP3 BP1 BP2 PS1 PS2
PS3 PS4 PM1 PM3 PM5
PM4 PM6 PP1 PP2 PP3
BA1 PVS1

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.1154T>G (p.Leu385Arg) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes (PM2 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: PM2: This variant is absent from gnomAD (gnomAD v2.1.1). PP4: Variant meet PM2. PMID: 10422804 (Loubser et al., 1999), South Africa - 1 case who fulfills Simon-Broome criteria for FH.

Met criteria codes

PM2	✔	This variant is absent from gnomAD (gnomAD v2.1.1).
PP4	✔	Variant meet PM2. PMID: 10422804 (Loubser et al., 1999), South Africa - 1 case who fulfills Simon-Broome criteria for FH.

Not Met criteria codes

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
BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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
PS4		✖	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
PM5		✖	2 other missense variants in the same codon: - NM_000527.5(LDLR):c.1153C>G (p.Leu385Val) (ClinVar ID 251691) - Uncertain significance - insufficient evidence by these guidelines - NM_000527.5(LDLR):c.1154T>C (p.Leu385Pro) (ClinVar ID 440626) - Uncertain significance - insufficient evidence by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.
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
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
PP3	✖	REVEL = 0.687. It is not above 0.75, splicing evaluation needed. Functional data on splicing not available. A) variant not on limits. B) variant not on limits. C) variant not on limits. Variant is not predicted to alter splicing
BA1	✖	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

Curation History

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