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.937T>C (p.Cys313Arg)

Version: 1.0

CA10585207

251537 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: f83f99f0-226d-4d9d-9eb2-e32d2fbe6149
Approved on: 2023/4/28
Published on: 2023/4/30

HGVS expressions

NM_000527.5:c.937T>C
NM_000527.5(LDLR):c.937T>C (p.Cys313Arg)
NC_000019.10:g.11107511T>C
CM000681.2:g.11107511T>C
NC_000019.9:g.11218187T>C
CM000681.1:g.11218187T>C
NC_000019.8:g.11079187T>C
NG_009060.1:g.23131T>C
ENST00000252444.10:c.1195T>C
ENST00000559340.2:c.937T>C
ENST00000560467.2:c.937T>C
ENST00000558518.6:c.937T>C
ENST00000252444.9:c.1191T>C
ENST00000455727.6:c.433T>C
ENST00000535915.5:c.814T>C
ENST00000545707.5:c.556T>C
ENST00000557933.5:c.937T>C
ENST00000558013.5:c.937T>C
ENST00000558518.5:c.937T>C
ENST00000558528.1:n.452T>C
ENST00000560467.1:c.537T>C
NM_000527.4:c.937T>C
NM_001195798.1:c.937T>C
NM_001195799.1:c.814T>C
NM_001195800.1:c.433T>C
NM_001195803.1:c.556T>C
NM_001195798.2:c.937T>C
NM_001195799.2:c.814T>C
NM_001195800.2:c.433T>C
NM_001195803.2:c.556T>C

Likely Pathogenic

Met criteria codes 5

PM1 PM2 PS4_Supporting PP3 PP4

Not Met criteria codes 2

PM5 PS3

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.937T>C (p.Cys313Arg) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM2, PP3, PM1, PP4, PS4_Supporting) 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: This variant is absent from gnomAD (gnomAD v2.1.1). PP3: REVEL=0.978. PM1: Variant meets PM2 and is one of the cysteine residues listed involving disulfide bone formation. PP4: Variant meets PM2 and is identified in ˃1 index cases who fulfil criteria for FH after alternative causes of high cholesterol were excluded. PS4_Supporting: Variant meets PM2 and is identified in 2 unrelated index cases reported in PubMed: one case fulfil Simon Broome criteria for definite or possible FH in PMID 22881376, reported by Usifo et al, 2012, from British Heart Foundation Laboratories, University College London, UK; one case fulfil DLCN ≥6 in PMID 19318025 reported by Alonso et al, 2009, from Lipid Clinic, Fundacion Jimenez Diaz, Spain. PS3 not met: Functional data is not available. PM5 not met: Three other missense variants at same codon: NM_000527.5 (LDLR):c.937T>G (p.Cys313Gly), ClinVarID 251538, is classified as Uncertain significance; NM_000527.5 (LDLR):c.939C>G (p.Cys313Trp), ClinVarID 251540, is classified as Likely Pathogenic; NM_000527.5 (LDLR):c.938G>A (p.Cys313Tyr), ClinVarID 226339, is classified as Likely Pathogenic by these guidelines, therefore PM5 is not met.

Met criteria codes

PM1	✔	Variant meets PM2 and is one of the cysteine residues listed involving disulfide bone formation.
PM2	✔	This variant is absent from gnomAD (gnomAD v2.1.1).
PS4_Supporting	✔	Variant meets PM2 and is identified in 2 unrelated index cases reported in PubMed: one case fulfil Simon Broome criteria for definite or possible FH in PMID 22881376, reported by Usifo et al, 2012, from British Heart Foundation Laboratories, University College London, UK; one case fulfil DLCN ≥6 in PMID 19318025 reported by Alonso et al, 2009, from Lipid Clinic, Fundacion Jimenez Diaz, Spain.
PP3	✔	REVEL=0.978.
PP4	✔	Variant meets PM2 and is identified in ˃1 index cases who fulfil criteria for FH after alternative causes of high cholesterol were excluded.

Not Met criteria codes

PM5		✖	Three other missense variants at same codon: NM_000527.5 (LDLR):c.937T>G (p.Cys313Gly), ClinVarID 251538, is classified as Uncertain significance; NM_000527.5 (LDLR):c.939C>G (p.Cys313Trp), ClinVarID 251540, is classified as Likely Pathogenic; NM_000527.5 (LDLR):c.938G>A (p.Cys313Tyr), ClinVarID 226339, is classified as Likely Pathogenic by these guidelines, therefore PM5 is not met.
PS3		✖	Functional data is not available.

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.