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.727T>C (p.Cys243Arg)

Version: 1.0

CA10585105

251425 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 9e2e98d3-6ac1-41d2-826f-87825e2b6139
Approved on: 2023/4/28
Published on: 2023/5/1

HGVS expressions

NM_000527.5:c.727T>C
NM_000527.5(LDLR):c.727T>C (p.Cys243Arg)
NC_000019.10:g.11106597T>C
CM000681.2:g.11106597T>C
NC_000019.9:g.11217273T>C
CM000681.1:g.11217273T>C
NC_000019.8:g.11078273T>C
NG_009060.1:g.22217T>C
ENST00000252444.10:c.985T>C
ENST00000559340.2:c.727T>C
ENST00000560467.2:c.727T>C
ENST00000558518.6:c.727T>C
ENST00000252444.9:c.981T>C
ENST00000455727.6:c.314-795T>C
ENST00000535915.5:c.604T>C
ENST00000545707.5:c.346T>C
ENST00000557933.5:c.727T>C
ENST00000558013.5:c.727T>C
ENST00000558518.5:c.727T>C
ENST00000558528.1:n.242T>C
ENST00000560467.1:c.327T>C
NM_000527.4:c.727T>C
NM_001195798.1:c.727T>C
NM_001195799.1:c.604T>C
NM_001195800.1:c.314-795T>C
NM_001195803.1:c.346T>C
NM_001195798.2:c.727T>C
NM_001195799.2:c.604T>C
NM_001195800.2:c.314-795T>C
NM_001195803.2:c.346T>C

Likely Pathogenic

Met criteria codes 5

PP3 PP4 PM2 PM1 PS4_Supporting

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.727T>C (p.Cys243Arg) variant is classified as likely pathogenic for Familial Hypercholesterolemia by applying evidence code PM1, PM2, PP3, PP4 and 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 = 0.966 PM1 - Variant meets PM2 and alters Cys243, one of the cysteine residues listed. PS4_Supporting - Variant meets PM2 and is identified in 2 index cases who fullfill DLCN≥6 criteria for FH from Research Lab of Molecular Genetics of Lipid Metabolism and PMID: 28502510. PP4 - Variant meets PM2 and is identified in 2 index cases who fullfill DLCN≥6 criteria for FH from Research Lab of Molecular Genetics of Lipid Metabolism after alternative cause of high cholesterol were excluded.

Met criteria codes

PP3	✔	REVEL = 0.966
PP4	✔	Variant meets PM2 and is identified in 2 index cases who fullfill DLCN≥6 criteria for FH from Research Lab of Molecular Genetics of Lipid Metabolism after alternative cause of high cholesterol were excluded.
PM2	✔	This variant is absent from gnomAD (gnomAD v2.1.1).
PM1	✔	Variant meets PM2 and alters Cys243, one of the cysteine residues listed.
PS4_Supporting	✔	Variant meets PM2 and is identified in 2 index cases who fullfill DLCN≥6 criteria for FH from Research Lab of Molecular Genetics of Lipid Metabolism and PMID: 28502510.

Curation History

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