

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

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HGVS expressions

NM_000527.5(LDLR):c.727T>C (p.Cys243Arg)

NM_000527.5:c.727T>C

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

PP3PP4PM2PM1PS4_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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