

Variant: *NM_000527.5(LDLR):c.709C>T (p.Arg237Cys)*

Version: 1.0

CA10585102 [↗](#)

251421 (ClinVar) [↗](#)

Gene: LDLR ([HGNC:3949](#))

Condition: hypercholesterolemia, familial ([MONDO:0007750](#))

Inheritance Mode: Semidominant inheritance

UUID: 0f079b07-dce5-4c8b-9a40-120dc80b5e35

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HGVS expressions

NM_000527.5(LDLR):c.709C>T (p.Arg237Cys)

NM_000527.5:c.709C>T

NC_000019.10:g.11106579C>T

CM000681.2:g.11106579C>T

NC_000019.9:g.11217255C>T

CM000681.1:g.11217255C>T

NC_000019.8:g.11078255C>T

NG_009060.1:g.22199C>T

ENST00000252444.10:c.967C>T

ENST00000559340.2:c.709C>T

ENST00000560467.2:c.709C>T

ENST00000558518.6:c.709C>T

ENST00000252444.9:c.963C>T

ENST00000455727.6:c.314-813C>T

ENST00000535915.5:c.586C>T

ENST00000545707.5:c.328C>T

ENST00000557933.5:c.709C>T

ENST00000558013.5:c.709C>T

ENST00000558518.5:c.709C>T

ENST00000558528.1:n.224C>T

ENST00000560467.1:c.309C>T

NM_000527.4:c.709C>T

NM_001195798.1:c.709C>T

NM_001195799.1:c.586C>T

NM_001195800.1:c.314-813C>T

NM_001195803.1:c.328C>T

NM_001195798.2:c.709C>T

NM_001195799.2:c.586C>T

NM_001195800.2:c.314-813C>T

NM_001195803.2:c.328C>T

Uncertain Significance

Met criteria codes **3**

PP4

PM2

PS4_Supporting

Not Met criteria codes **3**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.709C>T (p.Arg237Cys) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence code PM2, PS4_Moderate and PP4 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 - PopMax MAF = 0.00009799 (0.01%) in South Asian exomes (gnomAD v2.1.1). PS4_Supporting - Variant meets PM2 and is reported in 3 unrelated index cases, two with possible SB criteria (PMID 20236128 and Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)), one with DLCN >= 6 criteria (PMID 30293936). PP4 - Variant meets PM2 and is reported in 3 unrelated index cases, two with possible SB criteria (PMID 20236128 and Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)), one with DLCN >= 6 criteria (PMID 30293936).

Met criteria codes

PP4			Variant meets PM2 and is reported in 3 unrelated index cases, two with possible SB criteria (PMID 20236128 and Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)), one with DLCN >= 6 criteria (PMID 30293936).
PM2			PopMax MAF = 0.00009799 (0.01%) in South Asian exomes (gnomAD v2.1.1).
PS4_Supporting			Variant meets PM2 and is reported in 3 unrelated index cases, two with possible SB criteria (PMID 20236128 and Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation)), one with DLCN >= 6 criteria (PMID 30293936).

Not Met criteria codes

PS1			no other missense variants at same codon with same aa change
PP3			REVEL = 0.743. It is not above 0.75, plicing evaluation required. There is no functional data on splicing available. Variant is exonic, and at least 50 bp upstream from canonical donor site but does not create an AG, so PP3 is not met.
PM5			There is one other missense variant in the same codon NM_000527.5(LDLR):c.710G>A (p.Arg237His). It is considered as Uncertain significance - insufficient evidence by this guidelines. PM5 is not met.

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