

Variant: *NM_000527.5(LDLR):c.2547+5G>C*

Version: 1.0

[CA10585882](#)

[252354 \(ClinVar\)](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: c11995af-6401-43d3-aef9-3a20a29d544c

Approved on: 2023-04-26

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HGVS expressions

NM_000527.5:c.2547+5G>C
NM_000527.5(LDLR):c.2547+5G>C
NC_000019.10:g.11129675G>C
CM000681.2:g.11129675G>C
NC_000019.9:g.11240351G>C
CM000681.1:g.11240351G>C
NC_000019.8:g.11101351G>C
NG_009060.1:g.45295G>C
ENST00000252444.10:c.2805+5G>C
ENST00000559340.2:c.*616+5G>C
ENST00000560467.2:c.2427+5G>C
ENST00000558518.6:c.2547+5G>C
ENST00000252444.9:c.2801+5G>C
ENST00000455727.6:c.2043+5G>C
ENST00000535915.5:c.2424+5G>C
ENST00000545707.5:c.2013+5G>C
ENST00000557933.5:c.2609+5G>C
ENST00000558013.5:c.2547+5G>C
ENST00000558518.5:c.2547+5G>C
ENST00000560628.1:n.108+2021G>C
NM_000527.4:c.2547+5G>C
NM_001195798.1:c.2547+5G>C
NM_001195799.1:c.2424+5G>C
NM_001195800.1:c.2043+5G>C
NM_001195803.1:c.2013+5G>C
NM_001195798.2:c.2547+5G>C
NM_001195799.2:c.2424+5G>C
NM_001195800.2:c.2043+5G>C
NM_001195803.2:c.2013+5G>C

Uncertain Significance

Met criteria codes **3**

PP3 PP4 PM2

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.2547+5G>C variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PP3 and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 26 April 2023. The supporting evidence is as follows: **PM2:** This variant is absent from gnomAD (gnomAD v2.1.1). **PP3:** No REVEL, splicing evaluation required. Functional data on splicing not available. A) variant located at -3 to +6 from canonical donor splice site. MES scores: canonical site variant = 3.74; canonical site wt = 11.11. Ratio variant/wt canonical donor: $3.74/11.11 = 0.34$ --- it is below 0.8 Variant is predicted to alter splicing. **PP4:** Variant meet PM2 and is identified in 1 index case who fulfils Simon Broome criteria for FH (PMID 20809525, Marduel et al. 2010) after alternative causes of high cholesterol are excluded.

Met criteria codes

PP3	 	PP3 - No REVEL, splicing evaluation required. Functional data on splicing not available. A) variant located at -3 to +6 from canonical donor splice site. MES scores: canonical site variant = 3.74; canonical site wt = 11.11. Ratio variant/wt canonical donor: $3.74/11.11 = 0.34$ --- it is below 0.8 Variant is predicted to alter splicing.
PP4	 	Variant meet PM2 and is identified in 1 index case who fulfils SB criteria for FH PMID: 20809525 after alternative causes of high cholesterol are excluded.
PM2	 	This variant is absent from gnomAD (gnomAD v2.1.1).

Curation History [↗](#)

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