

Variant: NM_000527.5(LDLR):c.1056C>T (p.Cys352=)

Version: 1.0

CA031425 [↗](#)

413780 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: e2aa03b0-4037-4694-9c5e-a098dab6b717

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HGVS expressions

NM_000527.5:c.1056C>T

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NC_000019.10:g.11110767C>T

CM000681.2:g.11110767C>T

NC_000019.9:g.11221443C>T

CM000681.1:g.11221443C>T

NC_000019.8:g.11082443C>T

NG_009060.1:g.26387C>T

ENST00000252444.10:c.1314C>T

ENST00000559340.2:c.1056C>T

ENST00000560467.2:c.941-747C>T

ENST00000558518.6:c.1056C>T

ENST00000252444.9:c.1310C>T

ENST00000455727.6:c.552C>T

ENST00000535915.5:c.933C>T

ENST00000545707.5:c.675C>T

ENST00000557933.5:c.1056C>T

ENST00000558013.5:c.1056C>T

ENST00000558518.5:c.1056C>T

ENST00000560173.1:n.55C>T

ENST00000560467.1:c.541-747C>T

NM_000527.4:c.1056C>T

NM_001195798.1:c.1056C>T

NM_001195799.1:c.933C>T

NM_001195800.1:c.552C>T

NM_001195803.1:c.675C>T

NM_001195798.2:c.1056C>T

NM_001195799.2:c.933C>T

NM_001195800.2:c.552C>T

NM_001195803.2:c.675C>T

Benign

Met criteria codes3

BP4BP7BA1

Not Met criteria codes11

BS2BS1BS4BS3PS3PS4PP1PP3PP4PM1PM2

Evidence Links0

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.1056C>T (p.Cys352=) variant is classified as Benign for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes BA1, BP4 and BP7 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 28 March 2025. The supporting evidence is as follows: BA1: FAF = 0.007247 (0.7%) in East Asian exomes; since FAF ≥0.5% (gnomAD v4.1.0), BA1 is met. BP4: No REVEL score. Splicing evaluation is required. Functional data on splicing not available. A) not on limits, B) it creates a GT --- MES scores: de novo donor = -3.87, authentic donor = 5.88 --- de novo score is negative, so it is not used. Variant is not predicted to alter splicing, BP4 is met. BP7: Variant is synonymous and meets BP4.

Met criteria codes

BP4			No REVEL found. Splicing evaluation is required. Functional data on splicing not available. A) not on limits, B) it creates a GT --- MES scores: de novo donor = -3.87, authentic donor = 5.88 --- de novo score is negative, so it is not used. Variant is not predicted to alter splicing, BP4 is met.
BP7			Variant is synonymous and meets BP4.
BA1			FAF = 0.007247 (0.7%) in east asian exomes, since FAF≥0.5% (gnomAD v4.0) so BA1 is met.

Not Met criteria codes

BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			not met (no information or reports of functional data).

