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.1705+2T>C

Version: 1.2

CA404089507

440656 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 54c85436-b1d2-492c-8f22-a6e78eb8c415
Approved on: 2026/1/23
Published on: 2026/7/14

HGVS expressions

NM_000527.5:c.1705+2T>C
NM_000527.5(LDLR):c.1705+2T>C
NC_000019.10:g.11116214T>C
CM000681.2:g.11116214T>C
NC_000019.9:g.11226890T>C
CM000681.1:g.11226890T>C
NC_000019.8:g.11087890T>C
NG_009060.1:g.31834T>C
ENST00000252444.10:c.1963+2T>C
ENST00000559340.2:c.1705+2T>C
ENST00000560467.2:c.1585+2T>C
ENST00000558518.6:c.1705+2T>C
ENST00000252444.9:c.1959+2T>C
ENST00000455727.6:c.1201+2T>C
ENST00000535915.5:c.1582+2T>C
ENST00000545707.5:c.1324+2T>C
ENST00000557933.5:c.1705+2T>C
ENST00000558013.5:c.1705+2T>C
ENST00000558518.5:c.1705+2T>C
ENST00000559340.1:c.426+2T>C
NM_000527.4:c.1705+2T>C
NM_001195798.1:c.1705+2T>C
NM_001195799.1:c.1582+2T>C
NM_001195800.1:c.1201+2T>C
NM_001195803.1:c.1324+2T>C
NM_001195798.2:c.1705+2T>C
NM_001195799.2:c.1582+2T>C
NM_001195800.2:c.1201+2T>C
NM_001195803.2:c.1324+2T>C

Likely Pathogenic

Met criteria codes 2

PVS1 PM2

Not Met criteria codes 1

PP4

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

Evidence Links 0

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.1705+2T>C variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PVS1 and PM2 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on January 23, 2026. The supporting evidence is as follows: PM2: This variant is absent from gnomAD v4.1.0. PVS1: Variant is in canonical +2 GT splice site that predicts exon 11 skipping and disruption to reading frame.

Met criteria codes

PVS1		✔	Variant is in canonical +2 GT splice site that predict a frameshift in exon 11
PM2		✔	This variant is absent from gnomAD v4.1.0

Not Met criteria codes

PP4		✖	No cases of the variant segregating in FH were found in the literature.

Curation History

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