

Variant: *NM_000527.5(LDLR):c.1504G>T (p.Asp502Tyr)*

Version: 1.0

[CA10585485](#) 

[251877 \(ClinVar\)](#) 

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

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

Inheritance Mode: Semidominant inheritance

UUID: 158831f7-f155-4b50-97d9-9f1c74307cf3

Approved on: 2025-02-28

Published on: 2025-04-08

HGVS expressions

NM_000527.5:c.1504G>T

NM_000527.5(LDLR):c.1504G>T (p.Asp502Tyr)

NC_000019.10:g.11113680G>T

CM000681.2:g.11113680G>T

NC_000019.9:g.11224356G>T

CM000681.1:g.11224356G>T

NC_000019.8:g.11085356G>T

NG_009060.1:g.29300G>T

ENST00000252444.10:c.1762G>T

ENST00000559340.2:c.1504G>T

ENST00000560467.2:c.1384G>T

ENST00000558518.6:c.1504G>T

ENST00000252444.9:c.1758G>T

ENST00000455727.6:c.1000G>T

ENST00000535915.5:c.1381G>T

ENST00000545707.5:c.1123G>T

ENST00000557933.5:c.1504G>T

ENST00000558013.5:c.1504G>T

ENST00000558518.5:c.1504G>T

ENST00000559340.1:c.225G>T

NM_000527.4:c.1504G>T

NM_001195798.1:c.1504G>T

NM_001195799.1:c.1381G>T

NM_001195800.1:c.1000G>T

NM_001195803.1:c.1123G>T

NM_001195798.2:c.1504G>T

NM_001195799.2:c.1381G>T

NM_001195800.2:c.1000G>T

NM_001195803.2:c.1123G>T

Uncertain Significance

Met criteria codes **2**

PP4 PM2

Not Met criteria codes **1**

PP3

Expert Panel

Familial Hypercholesterolemia VCEP 

Criteria Specification Information

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1504G>T p.(Asp502Tyr) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2 and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on February 28, 2025. PM2: This variant is absent from gnomAD (gnomAD v4.1.0). PP4: Variant meets PM2 and is identified in one FH case from The Netherlands fulfilling internationally accepted criteria, after alternative causes of high cholesterol were excluded, in PMID 11810272 (Fouchier et al., 2001).

Met criteria codes**PP4**

PP4: Variant meets PM2 and is identified in one FH case from The Netherlands fulfilling internationally accepted criteria (Defesche 2000), after alternative causes of high cholesterol were excluded (PMID: 11810272).

PM2

This variant is absent from gnomAD (gnomAD v4.1.0).

Not Met criteria codes**PP3**

REVEL = 0.699 creates GT: >var de novo TGC GTATAC MAXENT: -11.90 >canonical TGGgtgcgt MAXENT: 5.46 negative 1 AG nearby >wt TCTCTGTTGCGGATACCAAGGGC MAXENT: 1.62 >var TCTCTGTTGCGTATACCAAGGGC MAXENT: 4.50 >canonical cttctctcctcctgcctcagCAC MAXENT: 6.76 Ratio variant cryptic/wt cryptic: 4.50/1.62 = 2.78 --- it is above 1.1 Ratio variant cryptic/canonical acceptor/donor: 4.50/6.76 = 0.666 --- it is NOT above 0.9"

Curation History [↗](#)

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