

Variant: NM_000527.5(LDLR):c.1244A>G (p.Asp415Gly)

Version: 1.0

CA10585372 [↗](#)

251749 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 6aafd8e9-dd32-4827-ac63-ea9349dd174e

Approved on: 2023/6/23

Published on: 2025/6/30

HGVS expressions

NM_000527.5(LDLR):c.1244A>G (p.Asp415Gly)

NM_000527.5:c.1244A>G

NC_000019.10:g.11113335A>G

CM000681.2:g.11113335A>G

NC_000019.9:g.11224011A>G

CM000681.1:g.11224011A>G

NC_000019.8:g.11085011A>G

NG_009060.1:g.28955A>G

ENST00000252444.10:c.1502A>G

ENST00000559340.2:c.1244A>G

ENST00000560467.2:c.1124A>G

ENST00000558518.6:c.1244A>G

ENST00000252444.9:c.1498A>G

ENST00000455727.6:c.740A>G

ENST00000535915.5:c.1121A>G

ENST00000545707.5:c.863A>G

ENST00000557933.5:c.1244A>G

ENST00000558013.5:c.1244A>G

ENST00000558518.5:c.1244A>G

ENST00000560173.1:n.243A>G

ENST00000560467.1:c.724A>G

NM_000527.4:c.1244A>G

NM_001195798.1:c.1244A>G

NM_001195799.1:c.1121A>G

NM_001195800.1:c.740A>G

NM_001195803.1:c.863A>G

NM_001195798.2:c.1244A>G

NM_001195799.2:c.1121A>G

NM_001195800.2:c.740A>G

NM_001195803.2:c.863A>G

Likely Pathogenic

Met criteria codes 4

PP1_ModeratePP4PM2PS4_Supporting

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.1244A>G (p.Asp415Gly) variant is classified as Likely Pathogenic, for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PS4_Moderate, PP1_Moderate and PP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 23 June 2023. The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v2.1.1). PS4_Supporting, PP4: Variant meets PM2 and is identified in 2 unrelated cases who fulfill criteria for FH (at least 1 case from PMID 11810272 (Fouchier et al., 2001), The Netherlands; 1 case from PMID 10978268 (Bertolini et al., 2000), Italy). PP1_Moderate: Variant segregates with FH phenotype in at least 5 informative meiosis (minimum 4) from 1 family in PMID 10978268 (Bertolini et al., 2000), Italy.

Met criteria codes

PP1_Moderate	<div><div>i</div><div>✓</div></div>	- PP1_Moderate: Variant segregates with FH phenotype in at least 5 informative meiosis (minimum 4) from 1 family from PMID: 10978268.
PP4	<div><div>i</div><div>✓</div></div>	- PP4: Variant meets PM2 and is identified in at least 1 index case fulfilling Simon-Broome criteria for (possible) FH, after alternative causes of high cholesterol are excluded from PMID: 11810272 and 10978268.
PM2	<div><div>i</div><div>✓</div></div>	- PM2: This variant is absent from gnomAD (gnomAD v2.1.1).
PS4_Supporting	<div><div>i</div><div>✓</div></div>	- PS4_Supporting: Variant meets PM2 and is identified in 2 unrelated cases who fulfil specific criteria for FH: at least 1 index fulfilling Simon Broome criteria for definite or possible FH from PMID:11810272; and 1 index case fulfilling Simon Broome criteria from PMID:10978268.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.