

Variant: *NM_000527.5(LDLR):c.1204TTC[1] (p.Phe403del)*

Version: 1.0

CA10585356 [↗](#)

251731 (ClinVar) [↗](#)

Gene: [LDLR](#)

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

Inheritance Mode: Semidominant inheritance

UUID: 5f27e072-31eb-415e-a56b-be4715f15dab

Approved on: 2023/1/27

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HGVS expressions

NM_000527.5(LDLR):c.1204TTC[1] (p.Phe403del)

NM_000527.5:c.1204TTC[1]

NC_000019.10:g.11113298_11113300del

CM000681.2:g.11113298_11113300del

NC_000019.9:g.11223974_11223976del

CM000681.1:g.11223974_11223976del

NC_000019.8:g.11084974_11084976del

NG_009060.1:g.28918_28920del

ENST00000252444.10:c.1465_1467del

ENST00000559340.2:c.1207_1209del

ENST00000560467.2:c.1087_1089del

ENST00000558518.6:c.1207_1209del

ENST00000252444.9:c.1461_1463del

ENST00000455727.6:c.703_705del

ENST00000535915.5:c.1084_1086del

ENST00000545707.5:c.826_828del

ENST00000557933.5:c.1207_1209del

ENST00000558013.5:c.1207_1209del

ENST00000558518.5:c.1207_1209del

ENST00000560173.1:n.206_208del

ENST00000560467.1:c.687_689del

NM_000527.4:c.1207_1209del

NM_001195798.1:c.1207_1209del

NM_001195799.1:c.1084_1086del

NM_001195800.1:c.703_705del

NM_001195803.1:c.826_828del

NM_000527.5:c.1207_1209del

NM_001195798.2:c.1207_1209del

NM_001195799.2:c.1084_1086del

NM_001195800.2:c.703_705del

NM_001195803.2:c.826_828del

Met criteria codes **4**

Likely Pathogenic

PM4

PM2

PS4_Supporting

PP4

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Not Met criteria codes 16

PM1 PM3 PM5 PM6 BS1
BS4 BS3 BS2 PS1 PS2 PS3
BP5 BP2 BA1 PP1 PP3

Evidence Links 0

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.1207_1209del (p.Phe403del) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PM4, PP4 and PS4_Supporting as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 27 January 2023. The supporting evidence is as follows: **PM2:** This variant is absent from gnomAD (v2.1.1). **PM4:** Variant meets PM2 and is an in-frame deletion. **PS4_Supporting, PP4:** Variant meets PM2 and was identified in at least 5 unrelated index cases who fulfill criteria for FH (4 patients from PMID 22698793 (Tichý et al., 2012) and 1 patient from PMID 11462246 (Nauck et al., 2001), reported as 1205delTCT).

Met criteria codes

PM4			PM4 - Variant meets PM2 and is an in frame deletion.
PM2			PM2 - Variant is absent from gnomAD (v2.1.1).
PS4_Supporting			PS4_Supporting - Variant meets PM2 and was identified in 4 patients (PMID: 22698793) with MEDPED score of FH and and in 1 patient (PMID 11462246) reported as 1205delTCT with TC 10.33 and LDL-C 8.03.
PP4			PP4 - Variant meets PM2 and was identified in at least 5 patients meeting clinical FH criteria (PMID: 22698793 and PMID 11462246), after alternative causes of high cholesterol were excluded.

Not Met criteria codes

PM1			PM2 is Met, but variant is not a missense in exon 4 or any of the 60 Cys residues listed. Not applicable.
PM3			Variant meets PM2 but is not identified in an index case with heterozygous or homozygous FH phenotype as well as LDLR variant, in trans, or APOB/PCSK9 variant classified as Pathogenic by these or general ACMG guidelines.
PM5			Not applicable
PM6			No de novo cases were identified.
BS1			Variant is absent from gnomAD (v2.1.1).

BS4			No information or report of segregation data/cases
BS3			There is no functional evidence in ClinVar for this variant
BS2			Variant not identified in normolipidemic individuals
PS1			Not applicable
PS2			No de novo cases were identified.
PS3			There is no functional evidence in ClinVar for this variant
BP5			not applicable
BP2			Variant meets PM2 but is not identified in an index case with heterozygous or homozygous FH phenotype as well as LDLR variant, in trans, or APOB/PCSK9 variant classified as Pathogenic by these or general ACMG guidelines.
BA1			Variant is absent from gnomAD (v2.1.1).
PP1			PP1 - no information or report of segregation data/cases
PP3			PP3 - No REVEL (not a missense variant). In silico prediction/evaluation (MaxEnsScan) is not recommended for indels.

Curation History 		
Showing 1 to 1 of 1 rows		

