

Variant: *NM_000527.5(LDLR):c.910G>T (p.Asp304Tyr)*

Version: 1.0

CA10585188 [↗](#)

251517 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: e9cc60ac-0473-4260-b304-f5a2afe680af

Approved on: 2021/6/8

Published on: 2021/6/24

HGVS expressions

NM_000527.5:c.910G>T

NM_000527.5(LDLR):c.910G>T (p.Asp304Tyr)

NC_000019.10:g.11107484G>T

CM000681.2:g.11107484G>T

NC_000019.9:g.11218160G>T

CM000681.1:g.11218160G>T

NC_000019.8:g.11079160G>T

NG_009060.1:g.23104G>T

ENST00000252444.10:c.1168G>T

ENST00000559340.2:c.910G>T

ENST00000560467.2:c.910G>T

ENST00000558518.6:c.910G>T

ENST00000252444.9:c.1164G>T

ENST00000455727.6:c.406G>T

ENST00000535915.5:c.787G>T

ENST00000545707.5:c.529G>T

ENST00000557933.5:c.910G>T

ENST00000558013.5:c.910G>T

ENST00000558518.5:c.910G>T

ENST00000558528.1:n.425G>T

ENST00000560467.1:c.510G>T

NM_000527.4:c.910G>T

NM_001195798.1:c.910G>T

NM_001195799.1:c.787G>T

NM_001195800.1:c.406G>T

NM_001195803.1:c.529G>T

NM_001195798.2:c.910G>T

NM_001195799.2:c.787G>T

NM_001195800.2:c.406G>T

NM_001195803.2:c.529G>T

Likely Pathogenic

Met criteria codes **4**

PM5_Strong PP3 PP4 PM2

Not Met criteria codes **22**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

PVS1

BS2

BS1

BS4

BS3

BP5

BP7

BP4

BP3

BP1

BP2

PS1

PS2

PS3

PS4

PP1

PP2

BA1

PM6

PM1

PM3

PM4

[Criteria Specifications for this VCEP](#)

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.910G>T (p.Asp304Tyr) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM5_Strong, PM2, PP3 and PP4) as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (<https://doi.org/10.1101/2021.03.17.21252755>). The supporting evidence is as follows: PM5_strong - Four more missense variants described in same codon, of which 2 variants classified as Pathogenic, so PM5_Strong is Met. PM2 - No population data was found for this variant in gnomAD (gnomAD v2.1.1). PP3 - REVEL = 0.982. PP4 - Variant meets PM2. Identified in 1 FH case who fulfills Simon-Broome criteria for FH in PMID 1301940.

Met criteria codes

PM5_Strong			Four more missense variants described in same codon: (1)NM_000527.4(LDLR):c.910G>C (p.Asp304His) (ClinVar ID 440612) - classified as Likely pathogenic by these guidelines (2)NM_000527.5(LDLR):c.910G>A (p.Asp304Asn) (ClinVar ID 3692) - classified as Pathogenic by these guidelines (3)NM_000527.4(LDLR):c.911A>T (p.Asp304Val) (ClinVar ID 440613) - classified as Likely pathogenic by these guidelines (4)NM_000527.5(LDLR):c.912C>G (p.Asp304Glu) (ClinVar ID 226336) - classified as Pathogenic by these guidelines --- 2 variants classified as Pathogenic, so PM5_Strong is Met
PP3			REVEL = 0.982. It is above 0.75, so PP3 is Met
PP4			Variant meets PM2. Identified in 1 FH case who fulfills Simon-Broome criteria for FH (plasma cholesterol levels over 600mg/dl and tendon xanthomas) in PMID 1301940. ---- PP4 is Met
PM2			No population data was found for this variant in gnomAD (gnomAD v2.1.1)

Not Met criteria codes

PVS1			Missense variant, PVS1 Not Met
BS2			no unaffected individuals identified with the variant, so BS2 is Not Met
BS1			No population data was found for this variant in gnomAD (gnomAD v2.1.1)
BS4			no family members were tested, so BS4 is Not Met

BS3			no functional assays performed, not applicable
BP5			Not applicable
BP7			Missense variant, so BP7 is not applicable
BP4			REVEL = 0.982. It is not below 0.15 and PP3 is Met, so BP4 is Not Met
BP3			Not applicable
BP1			Not applicable
BP2			no individuals with other variants and heterozygous phenotype were identified, so BP2 is Not Met
PS1			No variant described that leads to the same amino acid change, so PS1 is Not Met
PS2			no de novo cases were identified, so PS2 is Not Met
PS3			no functional assays performed, not applicable
PS4			Variant meets PM2. Variant identified in 1 index case fulfilling Simon-Broome criteria for FH from PMID: 1301940, so PS4 is Not Met
PP1			no family members were tested, so PP1 is Not Met
PP2			Not applicable
BA1			No population data was found for this variant in gnomAD (gnomAD v2.1.1)
PM6			no de novo cases were identified, so PM6 is Not Met
PM1			Missense at codon 304. PM2 is Met, but it is not exon 4 or any of the 60 Cys residues listed, so PM1 is Not Met
PM3			Variant meets PM2. Index case from PMID 1301940 has phenotype of Homozygous FH and is compound heterozygous with NM_000527.5(LDLR):c.932A>G (p.Lys311Arg) variant (ClinVar ID 251532) - classified as VUS by these guidelines. --- 2nd variant classified as VUS, so PM3 is Not Met
PM4			Missense variant, not applicable

▼

▼

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.