

Variant: *NM_000527.5(LDLR):c.911A>T (p.Asp304Val)*

Version: 1.0

CA404081041 [↗](#)

440613 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: ee4ebbf9-bdb8-49c2-bda1-a3d4eed13a24

Approved on: 2022/3/18

Published on: 2022/5/1

HGVS expressions

NM_000527.5(LDLR):c.911A>T (p.Asp304Val)

NM_000527.5:c.911A>T

NC_000019.10:g.11107485A>T

CM000681.2:g.11107485A>T

NC_000019.9:g.11218161A>T

CM000681.1:g.11218161A>T

NC_000019.8:g.11079161A>T

NG_009060.1:g.23105A>T

ENST00000252444.10:c.1169A>T

ENST00000559340.2:c.911A>T

ENST00000560467.2:c.911A>T

ENST00000558518.6:c.911A>T

ENST00000252444.9:c.1165A>T

ENST00000455727.6:c.407A>T

ENST00000535915.5:c.788A>T

ENST00000545707.5:c.530A>T

ENST00000557933.5:c.911A>T

ENST00000558013.5:c.911A>T

ENST00000558518.5:c.911A>T

ENST00000558528.1:n.426A>T

ENST00000560467.1:c.511A>T

NM_000527.4:c.911A>T

NM_001195798.1:c.911A>T

NM_001195799.1:c.788A>T

NM_001195800.1:c.407A>T

NM_001195803.1:c.530A>T

NM_001195798.2:c.911A>T

NM_001195799.2:c.788A>T

NM_001195800.2:c.407A>T

NM_001195803.2:c.530A>T

Uncertain Significance

Met criteria codes **3**

PM5

PM2

PP3

Not Met criteria codes **19**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

PM1	PM3	PM4	PM6	BS1	
BS4	BS3	BS2	PVS1	PS1	
PS2	PS3	PS4	BP7	BP4	BP2
BA1	PP1	PP4			

[Criteria Specifications for this VCEP](#)

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.911A>T (p.Asp304Val) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes PM2, PM5 and PP3 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: PM2 - This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is Met. PM5 - 4 other missense variants in the same codon: - NNM_000527.5(LDLR):c.910G>A (p.Asp304Asn) (ClinVar ID 3692) - Pathogenic by these guidelines - NM_000527.5(LDLR):c.910G>C (p.Asp304His) (ClinVar ID 440612) - VUS by these guidelines - NM_000527.5(LDLR):c.912C>G (p.Asp304Glu) (ClinVar ID 226336) - Likely pathogenic by these guidelines - NM_000527.5(LDLR):c.910G>T (p.Asp304Tyr) (ClinVar ID 251517) - Likely pathogenic by these guidelines There is 1 variant in the same codon classified as Pathogenic by these guidelines, so PM5 is Met. PP3 - REVEL = 0.985. It is above 0.75, so PP3 is Met.

Met criteria codes

PM5			4 other missense variants in the same codon: - NNM_000527.5(LDLR):c.910G>A (p.Asp304Asn) (ClinVar ID 3692) - Pathogenic by these guidelines - NM_000527.5(LDLR):c.910G>C (p.Asp304His) (ClinVar ID 440612) - VUS by these guidelines - NM_000527.5(LDLR):c.912C>G (p.Asp304Glu) (ClinVar ID 226336) - Likely pathogenic by these guidelines - NM_000527.5(LDLR):c.910G>T (p.Asp304Tyr) (ClinVar ID 251517) - Likely pathogenic by these guidelines There is 1 variant in the same codon classified as Pathogenic by these guidelines, so PM5 is Met.
PM2			This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is Met.
PP3			REVEL = 0.985. It is above 0.75, so PP3 is Met.

Not Met criteria codes

PM1			Variant meets PM2 but is not located in exon 4 or alters a cysteine residues, so PM1 is Not Met.
PM3			No case-level data available, so PM3 is Not Met.
PM4			Variant meets PM2 but is missense, so PM4 is Not Met.
PM6			No evidence added, so PM6 is Not Met.
BS1			No population data was found for this variant in gnomAD (gnomAD v2.1.1), so BS1 is Not Met.

BS4			No evidence added of non-segregation data, so BS4 is Not Met.
BS3			There is no functional studies reported for this variant, so BS3 is not met.
BS2			Case-control data not reported, so BS2 is Not Met.
PVS1			Variant is missense, so PVS1 is Not Met.
PS1			There is no other missense variants in the same codon, so PS1 is Not Met.
PS2			No evidence added, so PS2 is Not Met.
PS3			There is no functional studies reported for this variant, so PS3 is not met.
PS4			Variant meets PM2, but case-control data not reported, so PS4 is Not Met.
BP7			Variant is not synonymous, so BP7 is Not Met.
BP4			REVEL = 0.985. It is not below 0.50, so BP4 is Not Met.
BP2			No case-level data available, so BP2 is Not Met.
BA1			No population data was found for this variant in gnomAD (gnomAD v2.1.1), so BA1 is Not Met.
PP1			No evidence added of segregation data, so PP1 is Not Met.
PP4			Variant meets PM2 but evidence of phenotype data is not reported, so PP4 is Not Met.

Curation History 		
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