

Variant: *NM_000527.5(LDLR):c.1952A>T (p.Asp651Val)*

Version: 1.2

CA10585694 [↗](#)

252128 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 761b16f7-9cf4-42d6-a358-64a3b3108dd7

Approved on: 2023/3/20

Published on: 2023/3/31

HGVS expressions

NM_000527.5(LDLR):c.1952A>T (p.Asp651Val)

NM_000527.5:c.1952A>T

NC_000019.10:g.11120198A>T

CM000681.2:g.11120198A>T

NC_000019.9:g.11230874A>T

CM000681.1:g.11230874A>T

NC_000019.8:g.11091874A>T

NG_009060.1:g.35818A>T

ENST00000252444.10:c.2210A>T

ENST00000559340.2:c.*21A>T

ENST00000560467.2:c.1832A>T

ENST00000558518.6:c.1952A>T

ENST00000252444.9:c.2206A>T

ENST00000455727.6:c.1448A>T

ENST00000535915.5:c.1829A>T

ENST00000545707.5:c.1571A>T

ENST00000557933.5:c.1952A>T

ENST00000558013.5:c.1952A>T

ENST00000558518.5:c.1952A>T

ENST00000559340.1:c.533A>T

NM_000527.4:c.1952A>T

NM_001195798.1:c.1952A>T

NM_001195799.1:c.1829A>T

NM_001195800.1:c.1448A>T

NM_001195803.1:c.1571A>T

NM_001195798.2:c.1952A>T

NM_001195799.2:c.1829A>T

NM_001195800.2:c.1448A>T

NM_001195803.2:c.1571A>T

Uncertain Significance

Met criteria codes **2**

PP3 PM2

Not Met criteria codes **20**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

BS2

PVS1

BS1

BS4

BS3

BP4

BP3

BP2

PS1

PS2

PS3

PS4

BA1

PP1

PP4

PM1

PM3

PM5

PM4

PM6

Evidence Links

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- 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.1952A>T (p.Asp651Val) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes PM2 and PP3 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (<https://doi.org/10.1016/j.gim.2021.09.012>). The supporting evidence is as follows: PM2: This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is met. PP3: REVEL = 0.793. It is above 0.75, so PP3 is met.

Met criteria codes

PP3			REVEL = 0.793. It is above 0.75, so PP3 is met.
PM2			This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is met.

Not Met criteria codes

BS2			No data available.
PVS1			Not a null variant (nonsense, frameshift, canonical +/- 1 or 2 splice sites, initiation codon, single or multiexon deletion)
BS1			This variant is absent from gnomAD (gnomAD v2.1.1).
BS4			No data available.
BS3			No data available.
BP4			REVEL = 0.793 (>0.5)
BP3			Not a In-frame deletions/insertions variant
BP2			No data available.
PS1			No other missense variant in the same codon resulting in the same amino acid change.

PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No data available.
PS4			No data available.
BA1			This variant is absent from gnomAD (gnomAD v2.1.1).
PP1			No data available.
PP4			No data available.
PM1			Not in exon 4 and not a cysteine residue.
PM3			No data available.
PM5			2 other missense variants in the same codon: - NM_000527.5(LDLR):c.1951G>A (p.Asp651Asn) (ClinVar ID 183128) - Uncertain significance by these guidelines - NM_000527.5(LDLR):c.1951G>T (p.Asp651Tyr) (ClinVar ID 252127) - Uncertain significance by these guidelines There are no variant in the same codon classified as Pathogenic by these guidelines.
PM4			Not a In-frame deletions/insertions variant
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
   owing 1 to 3 of 3 rows		

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