

Variant: *NM_000527.5(LDLR):c.2T>C (p.Met1Thr)*

Version: 1.0

CA404071092 [↗](#)

441174 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 7f40ca33-9ff0-4ff1-93fb-6c6a4b1bd789

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HGVS expressions

NM_000527.5(LDLR):c.2T>C (p.Met1Thr)

NM_000527.5:c.2T>C

NC_000019.10:g.11089550T>C

CM000681.2:g.11089550T>C

NC_000019.9:g.11200226T>C

CM000681.1:g.11200226T>C

NC_000019.8:g.11061226T>C

NG_009060.1:g.5170T>C

ENST00000559340.2:c.2T>C

ENST00000560467.2:c.2T>C

ENST00000558518.6:c.2T>C

ENST00000455727.6:c.2T>C

ENST00000535915.5:c.2T>C

ENST00000545707.5:c.2T>C

ENST00000557933.5:c.2T>C

ENST00000557958.1:n.88T>C

ENST00000558013.5:c.2T>C

ENST00000558518.5:c.2T>C

ENST00000560502.5:n.88T>C

NM_000527.4:c.2T>C

NM_001195798.1:c.2T>C

NM_001195799.1:c.2T>C

NM_001195800.1:c.2T>C

NM_001195803.1:c.2T>C

NM_001195798.2:c.2T>C

NM_001195799.2:c.2T>C

NM_001195800.2:c.2T>C

NM_001195803.2:c.2T>C

NR_163945.1:n.110A>G

Likely Pathogenic

Met criteria codes **3**

PVS1_Moderate

PM2

PM5

Not Met criteria codes **10**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.2T>C (p.Met1Thr) variant is classified as Likely Pathogenic for Familial Hypercholesterolemia by applying evidence codes PM2, PVS1_Moderate, and PM5 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 - variant is absent from gnomAD (v2.1.1). PVS1_Moderate - variant is predicted to affect the initiation codon. PM5 - four other missense variants at this same codon have been reported, and one is Pathogenic: 1) NM_000527.5(LDLR):c.1A>C (p.Met1Leu) - Pathogenic by these guidelines. 2) NM_000527.5(LDLR):c.1A>G (p.Met1Val) - Likely pathogenic by these guidelines. 3) NM_000527.4(LDLR):c.3G>A (p.Met1Ile) - Likely pathogenic by these guidelines. 4) NM_000527.5(LDLR):c.3G>T (p.Met1Ile) - Likely pathogenic by these guidelines.

Met criteria codes

PVS1_Moderate			Variant is predicted to affect the initiation codon.
PM2			Variant is absent from gnomAD (v2.1.1).
PM5			Four other missense variants at this same codon have been reported, and one is Pathogenic: 1) NM_000527.5(LDLR):c.1A>C (p.Met1Leu) – Pathogenic by these guidelines. 2) NM_000527.5(LDLR):c.1A>G (p.Met1Val) - Likely pathogenic by these guidelines. 3) NM_000527.4(LDLR):c.3G>A (p.Met1Ile) - Likely pathogenic by these guidelines. 4) NM_000527.5(LDLR):c.3G>T (p.Met1Ile) - Likely pathogenic by these guidelines.

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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