

Variant: NM_000527.5(LDLR):c.1867A>G (p.Ile623Val)

Version: 1.0

CA037254 [↗](#)

252096 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 71c55d4d-b913-48cb-bb50-fdfa27e456bc

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HGVS expressions

NM_000527.5:c.1867A>G

NM_000527.5(LDLR):c.1867A>G (p.Ile623Val)

NC_000019.10:g.11120113A>G

CM000681.2:g.11120113A>G

NC_000019.9:g.11230789A>G

CM000681.1:g.11230789A>G

NC_000019.8:g.11091789A>G

NG_009060.1:g.35733A>G

ENST00000252444.10:c.2125A>G

ENST00000559340.2:c.1727A>G

ENST00000560467.2:c.1747A>G

ENST00000558518.6:c.1867A>G

ENST00000252444.9:c.2121A>G

ENST00000455727.6:c.1363A>G

ENST00000535915.5:c.1744A>G

ENST00000545707.5:c.1486A>G

ENST00000557933.5:c.1867A>G

ENST00000558013.5:c.1867A>G

ENST00000558518.5:c.1867A>G

ENST00000559340.1:c.448A>G

NM_000527.4:c.1867A>G

NM_001195798.1:c.1867A>G

NM_001195799.1:c.1744A>G

NM_001195800.1:c.1363A>G

NM_001195803.1:c.1486A>G

NM_001195798.2:c.1867A>G

NM_001195799.2:c.1744A>G

NM_001195800.2:c.1363A>G

NM_001195803.2:c.1486A>G

Uncertain Significance

Met criteria codes **2**

PP1 BS1

Not Met criteria codes **18**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

PS1

PS2

PS3

BA1

PP4

PM1

PM3

PM5

PM4

PM6

PM2

BS4

BS3

BS2

BP4

BP3

BP2

PVS1

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1867A>G (p.Ile623Val) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes BS1 and PP1 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: The supporting evidence is as follows: BS1: PopMax FAF= 0.002650 (0.265%) in East Asian exomes (gnomAD v2.1.1). PP1: Variant segregates with FH phenotype in 2 informative meioses in 1 family from Laboratory of Genetics and Molecular Cardiology, Brazil.

Met criteria codes

PP1			Variant segregates with FH phenotype in 2 informative meioses in 1 family from Laboratory of Genetics and Molecular Cardiology. So PP1 is met.
BS1			PopMax FAF= 0.002650 (0.265%) in East Asian exomes (gnomAD v2.1.1). So BS1 is met.

Not Met criteria codes

PS1			No other missense variant in the same codon with 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
BA1			PopMax FAF= 0.002650 (0.265%) in East Asian exomes (gnomAD v2.1.1)
PP4			Variant doesn't meet PM2.
PM1			Not in exon 4. Not a cysteine residue.
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			

1 other missense variant in the same codon: - NM_000527.5(LDLR):c.1868T>C (p.Ile623Thr) (ClinVar ID 369855) - Unknown significance by these guidelines There is no variant in the same codon classified as Pathogenic by these guidelines.

PM4			No in-frame deletions/insertions
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			PopMax MAF= 0.00356 (0.356%) in East Asians (gnomAD v2.1.1)
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No data available
BS2			Variant identified in 2 normolipidemic, untreated, unrelated adults from PMID 12837857
BP4			REVEL=0.742. It is above 0.5.
BP3			No in-frame deletions/insertions
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			Not a null variant

Curation History



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