The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000527.5(LDLR):c.2479G>A (p.Val827Ile)

Version: 1.0

CA023677

36462 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 7013887c-0f2d-4f01-93b1-32e2c36dc390
Approved on: 2021-06-22
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HGVS expressions

NM_000527.5:c.2479G>A
NM_000527.5(LDLR):c.2479G>A (p.Val827Ile)
NC_000019.10:g.11129602G>A
CM000681.2:g.11129602G>A
NC_000019.9:g.11240278G>A
CM000681.1:g.11240278G>A
NC_000019.8:g.11101278G>A
NG_009060.1:g.45222G>A
ENST00000252444.10:c.2737G>A
ENST00000559340.2:c.*548G>A
ENST00000560467.2:c.2359G>A
ENST00000558518.6:c.2479G>A
ENST00000252444.9:c.2733G>A
ENST00000455727.6:c.1975G>A
ENST00000535915.5:c.2356G>A
ENST00000545707.5:c.1945G>A
ENST00000557933.5:c.2541G>A
ENST00000558013.5:c.2479G>A
ENST00000558518.5:c.2479G>A
ENST00000560628.1:n.108+1948G>A
NM_000527.4:c.2479G>A
NM_001195798.1:c.2479G>A
NM_001195799.1:c.2356G>A
NM_001195800.1:c.1975G>A
NM_001195803.1:c.1945G>A
NM_001195798.2:c.2479G>A
NM_001195799.2:c.2356G>A
NM_001195800.2:c.1975G>A
NM_001195803.2:c.1945G>A

Uncertain Significance

Met criteria codes 2

PP1 PP3

Not Met criteria codes 24

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

PVS1 PS1 PS2 PS3 PS4
PP2 PP4 BA1 PM6 PM2
PM1 PM3 BS1 BS4 BS3
PM5 PM4 BS2 BP5 BP7
BP4 BP3 BP1 BP2

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.2479G>A (p.Val827Ile) variant is classified as variant of Uncertain significance for Familial Hypercholesterolemia by applying evidence codes (PP1 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: PP1 - Variant segregates with FH phenotype in 3 informative meiosis from Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation). PP3 - REVEL: 0,771. Score is above 0,75.

Met criteria codes

PP1	✔	Variant segregates with FH phenotype in 3 informative meiosis from Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation).
PP3	✔	REVEL: 0,771. Score is above 0,75.

Not Met criteria codes

PVS1	✖	Missense variant. Not applicable.
PS1	✖	No variant described that leads to the same amino acid change.
PS2	✖	No de novo cases were identified.
PS3	✖	No functional assays performed/found - not applicable.
PS4	✖	PM2 is not met. Not applicable.
PP2	✖	Not applicable.
PP4	✖	PM2 is not met. Not applicable.
BA1	✖	FAF = 0.0007719 (0.08%) in Latino exomes (gnomAD v2.1.1). FAF is not above 0.5%.
PM6	✖	No de novo cases were identified.

PM2	✖	PopMax MAF = 0.01649 (1.65%) in Ashkenazi Jewish exomes (gnomAD v2.1.1). MAF is not below 0.02%.
PM1	✖	Missense at codon 827 - it is not exon 4 or any of the 60 Cys residues listed. Not applicable.
PM3	✖	PM2 is not met. Not applicable.
BS1	✖	FAF = 0.0007719 (0.08%) in Latino exomes (gnomAD v2.1.1). FAF is not above 0.2%.
BS4	✖	insuficient information
BS3	✖	No functional assays performed/found - not applicable.
PM5	✖	No other missense variants classified as Pathogenic by these guidelines. Two missense variants described in the same codon (accessed 19 August 2020): (1)NM_000527.4(LDLR):c.2479G>T (p.Val827Phe) (ClinVar ID 375840) - VUS by these guidelines. (2)NM_000527.5(LDLR):c.2480T>A (p.Val827Asp) (ClinVar ID 963080) - VUS by these guidelines.
PM4	✖	Missense variant. Not applicable.
BS2	✖	Two unaffected heterozygous carriers from Molecular Genetics Laboratory (Centre for Cardiovascular Surgery and Transplantation). At least 3 htz unaffected carriers are needed for adding this point. BS2 not met.
BP5	✖	Not applicable.
BP7	✖	Missense variant. Not applicable.
BP4	✖	REVEL: 0,771. Score is not below 0,15.
BP3	✖	Not applicable.
BP1	✖	Not applicable.
BP2	✖	Not applicable.

Curation History

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