Variant: NM_000527.5(LDLR):c.907C>T (p.Arg303Trp)

Version: 1.0

CA023787

161281 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: c980a4eb-d83f-4657-b86a-2b67d5862466
Approved on: 2021-06-08
Published on: 2021-06-24

HGVS expressions

NM_000527.5:c.907C>T
NM_000527.5(LDLR):c.907C>T (p.Arg303Trp)
NC_000019.10:g.11107481C>T
CM000681.2:g.11107481C>T
NC_000019.9:g.11218157C>T
CM000681.1:g.11218157C>T
NC_000019.8:g.11079157C>T
NG_009060.1:g.23101C>T
ENST00000252444.10:c.1165C>T
ENST00000559340.2:c.907C>T
ENST00000560467.2:c.907C>T
ENST00000558518.6:c.907C>T
ENST00000252444.9:c.1161C>T
ENST00000455727.6:c.403C>T
ENST00000535915.5:c.784C>T
ENST00000545707.5:c.526C>T
ENST00000557933.5:c.907C>T
ENST00000558013.5:c.907C>T
ENST00000558518.5:c.907C>T
ENST00000558528.1:n.422C>T
ENST00000560467.1:c.507C>T
NM_000527.4:c.907C>T
NM_001195798.1:c.907C>T
NM_001195799.1:c.784C>T
NM_001195800.1:c.403C>T
NM_001195803.1:c.526C>T
NM_001195798.2:c.907C>T
NM_001195799.2:c.784C>T
NM_001195800.2:c.403C>T
NM_001195803.2:c.526C>T

Uncertain Significance

Met criteria codes 1

PP3

Not Met criteria codes 25

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

BS2 BS1 BS4 BS3 BP5 BP7
BP4 BP3 BP1 BP2 PS1 PS2
PS3 PS4 PP1 PP2 PP4 BA1
PM6 PM2 PM1 PM3 PM5
PM4 PVS1

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.907C>T (p.Arg303Trp) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes (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: PP3 - REVEL = 0.815. It is above 0.75, so PP3 is Met.

Met criteria codes

PP3	✔	REVEL = 0.815. It is above 0.75, so PP3 is Met

Not Met criteria codes

BS2	✖	no unaffected individuals identified with the variant, so BS2 is Not Met
BS1	✖	FAF = 0.0002884 (0.029%) in African/African American exomes (gnomAD v2.1.1). FAF is not above 0.2%, so BS1 is Not Met.
BS4	✖	no family members were tested, so BS4 is Not Met
BS3	✖	no functional assays performed, not applicable
BP5	✖	Not applicable
BP7	✖	Missense variant, so BP7 is not applicable
BP4	✖	REVEL = 0.815. It is not below 0.15 and PP3 is Met, so BP4 is Not Met
BP3	✖	Not applicable
BP1	✖	Not applicable
BP2	✖	not identified in individuals with other variants, so BP2 is Not Met

PS1	✖	No variant described that leads to the same amino acid change, so PS1 is Not Met
PS2	✖	no de novo cases were identified, so PS2 is Not Met
PS3	✖	no functional assays performed, not applicable
PS4	✖	variant does not meet PM2, so PS4 is Not Met
PP1	✖	no family members were tested, so PP1 is Not Met
PP2	✖	Not applicable
PP4	✖	Variant does not meet PM2, so PP4 is Not Met
BA1	✖	FAF = 0.0002884 (0.029%) in African/African American exomes (gnomAD v2.1.1). FAF is not above 0.5%, so BA1 is Not Met.
PM6	✖	no de novo cases were identified, so PM6 is Not Met
PM2	✖	PopMax MAF = 0.0004009 (0.04%) in African/African American exomes (gnomAD v2.1.1). MAF is not under 0.02%, so PM2 is Not Met.
PM1	✖	Missense at codon 303. PM2 is Not Met, it is not exon 4 or any of the 60 Cys residues listed, so PM1 is Not Met
PM3	✖	not identified in individuals with other variants, so PM3 is Not Met
PM5	✖	One more missense variant described in same codon: (1)NM_000527.4(LDLR):c.908G>A (p.Arg303Gln) (ClinVar ID 183101) - classified as VUS by these guidelines --- variant classified as VUS, so PM5 is Not Met
PM4	✖	Missense variant, not applicable
PVS1	✖	Missense variant, PVS1 Not Met

Curation History

owing 1 to 1 of 1 rows