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.2043C>G (p.Cys681Trp)

Version: 1.0

CA10585743

252188 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: c12a6a0d-1d06-4705-8036-67b2e5a31e81
Approved on: 2021/6/18
Published on: 2021/6/24

HGVS expressions

NM_000527.5(LDLR):c.2043C>G (p.Cys681Trp)
NM_000527.5:c.2043C>G
NC_000019.10:g.11120425C>G
CM000681.2:g.11120425C>G
NC_000019.9:g.11231101C>G
CM000681.1:g.11231101C>G
NC_000019.8:g.11092101C>G
NG_009060.1:g.36045C>G
ENST00000252444.10:c.2301C>G
ENST00000559340.2:c.*112C>G
ENST00000560467.2:c.1923C>G
ENST00000558518.6:c.2043C>G
ENST00000252444.9:c.2297C>G
ENST00000455727.6:c.1539C>G
ENST00000535915.5:c.1920C>G
ENST00000545707.5:c.1606+192C>G
ENST00000557933.5:c.2043C>G
ENST00000558013.5:c.2043C>G
ENST00000558518.5:c.2043C>G
NM_000527.4:c.2043C>G
NM_001195798.1:c.2043C>G
NM_001195799.1:c.1920C>G
NM_001195800.1:c.1539C>G
NM_001195803.1:c.1606+192C>G
NM_001195798.2:c.2043C>G
NM_001195799.2:c.1920C>G
NM_001195800.2:c.1539C>G
NM_001195803.2:c.1606+192C>G

Pathogenic

Met criteria codes 5

PP1_Strong PP3 PP4 PM2 PM1

Not Met criteria codes 21

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

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

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.2043C>G (p.Cys681Trp) variant is classified as Pathogenic for Familial Hypercholesterolemia by applying evidence codes (PP1_Strong, PM1, PM2, PP3 and PP4) 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_strong - Variant segregates with FH phenotype in 7 informative meioses in 1 family from PMID: 16092059. PM1 - Variant meets PM2 and is one of listed Cysteine. PM2 - No population data was found for this allele in gnomAD (gnomAD v2.1.1). PP3 - REVEL: 0,83. PP4 - Variant meet PM2. PMID: 16092059 - 1 case who fulfills Simon-Broome criteria for FH.

Met criteria codes

PP1_Strong	✔	Variant segregates with FH phenotype in 7 informative meioses in 1 family from PMID: 16092059.
PP3	✔	REVEL: 0,83. Score is above 0,75.
PP4	✔	Variant meet PM2. PMID: 16092059 - 1 case who fulfills Simon-Broome criteria for FH.
PM2	✔	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
PM1	✔	Variant meets PM2 and is one of listed Cysteine. S-S bond with Cys667.

Not Met criteria codes

BS2	✖	No unaffected individuals identified with the variant.
BS1	✖	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
BS4	✖	No non-segregations were identified/found.
BS3	✖	No functional assays performed/found - not applicable.
BP4	✖	REVEL: 0,83. Score is not below 0,50.
BP3	✖	Not applicable.

BP1	✖	Not applicable.
BP2	✖	Not identified in individuals with other variants.
PVS1	✖	Missense variant. Not applicable.
BP5	✖	Not applicable.
BP7	✖	Missense variant. Not applicable.
BA1	✖	No population data was found for this allele in gnomAD (gnomAD v2.1.1).
PS1	✖	Variant meets PM1, so not applicable.
PS2	✖	No de novo cases were identified.
PS3	✖	No functional assays performed/found - not applicable.
PS4	✖	PMID: 16092059 - 1 case with Simon-Broome criteria. At least 2 unrelated cases are needed for PS4.
PP2	✖	Not applicable.
PM6	✖	No de novo cases were identified.
PM3	✖	Not identified in individuals with other variants.
PM5	✖	Variant meets PM1, so not applicable.
PM4	✖	Missense variant. Not applicable.

Curation History

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