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.1055G>A (p.Cys352Tyr)

Version: 1.0

CA023408

36450 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 1b7719a1-ebea-4124-9925-8b5037b8efc0
Approved on: 2021-06-08
Published on: 2021-06-24

HGVS expressions

NM_000527.5:c.1055G>A
NM_000527.5(LDLR):c.1055G>A (p.Cys352Tyr)
NC_000019.10:g.11110766G>A
CM000681.2:g.11110766G>A
NC_000019.9:g.11221442G>A
CM000681.1:g.11221442G>A
NC_000019.8:g.11082442G>A
NG_009060.1:g.26386G>A
ENST00000252444.10:c.1313G>A
ENST00000559340.2:c.1055G>A
ENST00000560467.2:c.941-748G>A
ENST00000558518.6:c.1055G>A
ENST00000252444.9:c.1309G>A
ENST00000455727.6:c.551G>A
ENST00000535915.5:c.932G>A
ENST00000545707.5:c.674G>A
ENST00000557933.5:c.1055G>A
ENST00000558013.5:c.1055G>A
ENST00000558518.5:c.1055G>A
ENST00000560173.1:n.54G>A
ENST00000560467.1:c.541-748G>A
NM_000527.4:c.1055G>A
NM_001195798.1:c.1055G>A
NM_001195799.1:c.932G>A
NM_001195800.1:c.551G>A
NM_001195803.1:c.674G>A
NM_001195798.2:c.1055G>A
NM_001195799.2:c.932G>A
NM_001195800.2:c.551G>A
NM_001195803.2:c.674G>A

Likely Pathogenic

Met criteria codes 5

PP3 PP4 PM2 PM1 PS4_Supporting

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

Not Met criteria codes 21

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

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.1055G>A (p.Cys352Tyr) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM1, PM2, PP3, PP4 and PS4_Supporting) 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: PM1 - Variant meets PM2 and alters Cys340, one of the cysteine residues listed. PM2 - PopMax MAF = 0.00005782 (0.006%) in Latino/Admixed American exomes (gnomAD v2.1.1). PP3 - REVEL: 0,98. PP4 - Variant meets PM2. Identified in 1 FH case from Center of molecular biology and gene therapy who fulfills Simon-Broome criteria and in 1 FH case published in PMID: 30592178 who fulfills DLCN criteria. PS4_supporting - Variant meets PM2. Variant identified in 2 index cases with clinical FH criteria.

Met criteria codes

PP3	✔	REVEL: 0,98. Score is above 0,75.
PP4	✔	Variant meets PM2. Identified in 1 FH case from Center of molecular biology and gene therapy who fulfills Simon-Broome criteria and in 1 FH case published in PMID: 30592178 who fulfills DLCN criteria.
PM2	✔	PopMax MAF = 0.00005782 (0.006%) in Latino/Admixed American exomes (gnomAD v2.1.1). MAF is under 0.02%
PM1	✔	Variant meets PM2 and alters Cys340, one of the cysteine residues listed, so PM1 is met
PS4_Supporting	✔	Variant meets PM2. Variant identified in 2 index cases (1 case from Center of molecular biology and gene therapy with Simon-Broome criteria; 1 case in PMID: 30592178 with DLCN criteria).

Not Met criteria codes

BA1	✖	FAF = 0.000009580 (0.0009580%) in Latino/Admixed American exomes (gnomAD v2.1.1). FAF is not above 0.5%
BS1	✖	FAF = 0.000009580 (0.0009580%) in Latino/Admixed American exomes (gnomAD v2.1.1). FAF is not above 0.2%
BS4	✖	No variant negative family members were tested.
BS3	✖	No functional assays performed/found - not applicable.

BS2	✖	No unaffected individuals identified with the variant.
BP5	✖	Not applicable.
BP7	✖	Missense variant.
BP4	✖	REVEL: 0,98. Score is not below 0,15. PP3 met.
BP3	✖	not applicable
BP1	✖	Not applicable.
BP2	✖	Not identified in individuals with other variants.
PS1	✖	Variant meets PM1, so PS1 is not applicable
PS2	✖	No de novo cases were identified.
PS3	✖	No functional assays performed/found - not applicable.
PP1	✖	Variant segregates with phenotype in 1 informative meiosis in 1 family from GeneDx Inc. laboratory. Minimal number of meioses is 2.
PP2	✖	Not applicable.
PM6	✖	No de novo cases were identified.
PM3	✖	Not identified in individuals with other variants.
PM5	✖	Variant meets PM1, so PM5 is not applicable
PM4	✖	Missense variant.
PVS1	✖	Missense variant.

Curation History

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