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.858C>A (p.Ser286Arg)

Version: 1.0

CA029904

251488 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 7d35f7d3-b40a-4137-ace3-7d0c87f989f6
Approved on: 2022/1/19
Published on: 2022/6/30

HGVS expressions

NM_000527.5(LDLR):c.858C>A (p.Ser286Arg)
NM_000527.5:c.858C>A
NC_000019.10:g.11107432C>A
CM000681.2:g.11107432C>A
NC_000019.9:g.11218108C>A
CM000681.1:g.11218108C>A
NC_000019.8:g.11079108C>A
NG_009060.1:g.23052C>A
ENST00000252444.10:c.1116C>A
ENST00000559340.2:c.858C>A
ENST00000560467.2:c.858C>A
ENST00000558518.6:c.858C>A
ENST00000252444.9:c.1112C>A
ENST00000455727.6:c.354C>A
ENST00000535915.5:c.735C>A
ENST00000545707.5:c.477C>A
ENST00000557933.5:c.858C>A
ENST00000558013.5:c.858C>A
ENST00000558518.5:c.858C>A
ENST00000558528.1:n.373C>A
ENST00000560467.1:c.458C>A
NM_000527.4:c.858C>A
NM_001195798.1:c.858C>A
NM_001195799.1:c.735C>A
NM_001195800.1:c.354C>A
NM_001195803.1:c.477C>A
NM_001195798.2:c.858C>A
NM_001195799.2:c.735C>A
NM_001195800.2:c.354C>A
NM_001195803.2:c.477C>A

Likely Pathogenic

Met criteria codes 5

PM2 PS4_Supporting PP1 PP3 PP4

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

Not Met criteria codes 21

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

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.858C>A (p.Ser286Arg) variant is classified as Likely pathogenic for Familial Hypercholesterolemia by applying evidence codes (PM2, PS4_Supporting, PP1, PP3 and PP4) as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (https://doi.org/10.1016/j.gim.2021.09.012). The supporting evidence is as follows: PM2 - PopMax MAF = 0.00006155 (0.006155%) in European (non-Finnish) exomes+genomes (gnomAD v2.1.1). PS4_Supporting - Variant meets PM2 and is identified in 4 unrelated index cases who fulfil DLCN >=6 (1 case in PMID: 32770674; 2 cases from Robarts Research Institute) or SB definitive (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation). PP1 - Variant segregates with FH phenotype in 2 informative meiosis from 2 unrelated families (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation and 1 case from Robarts Research Institute). PP3 - REVEL = 0.766. PP4 - Variant meets PM2 and is identified in 4 index cases who fulfil DLCN >=6 (1 case in PMID: 32770674; 2 cases from Robarts Research Institute) or SB definitive (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation).

Met criteria codes

PM2	✔	PopMax MAF = 0.00006155 (0.006155%) in European (non-Finnish) exomes+genomes (gnomAD v2.1.1).
PS4_Supporting	✔	Variant meets PM2 and is identified in 4 unrelated index cases who fulfil DLCN >=6 (1 case in PMID: 32770674; 2 cases from Robarts Research Institute) or SB definitive (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation).
PP1	✔	Variant segregates with FH phenotype in 2 informative meiosis from 2 unrelated families (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation and 1 case from Robarts Research Institute)
PP3	✔	REVEL = 0.766.
PP4	✔	Variant meets PM2 and is identified in 4 index cases who fulfil DLCN >=6 (1 case in PMID: 32770674; 2 cases from Robarts Research Institute) or SB definitive (1 case from Molecular Genetics Laboratory of Centre for Cardiovascular Surgery and Transplantation).

Not Met criteria codes

PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PVS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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