Variant: NM_000527.5(LDLR):c.2140+5G>A

Version: 1.0

CA023645

36460 (ClinVar)

Gene: LDLR (HGNC:3949)
Condition: hypercholesterolemia, familial (MONDO:0007750)
Inheritance Mode: Semidominant inheritance
UUID: 56e1a7d8-b14a-4759-be2e-3a9ea6668dec
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HGVS expressions

NM_000527.5:c.2140+5G>A
NM_000527.5(LDLR):c.2140+5G>A
NC_000019.10:g.11120527G>A
CM000681.2:g.11120527G>A
NC_000019.9:g.11231203G>A
CM000681.1:g.11231203G>A
NC_000019.8:g.11092203G>A
NG_009060.1:g.36147G>A
ENST00000252444.10:c.2398+5G>A
ENST00000559340.2:c.*209+5G>A
ENST00000560467.2:c.2020+5G>A
ENST00000558518.6:c.2140+5G>A
ENST00000252444.9:c.2394+5G>A
ENST00000455727.6:c.1636+5G>A
ENST00000535915.5:c.2017+5G>A
ENST00000545707.5:c.1606+294G>A
ENST00000557933.5:c.2140+5G>A
ENST00000558013.5:c.2140+5G>A
ENST00000558518.5:c.2140+5G>A
NM_000527.4:c.2140+5G>A
NM_001195798.1:c.2140+5G>A
NM_001195799.1:c.2017+5G>A
NM_001195800.1:c.1636+5G>A
NM_001195803.1:c.1606+294G>A
NM_001195798.2:c.2140+5G>A
NM_001195799.2:c.2017+5G>A
NM_001195800.2:c.1636+5G>A
NM_001195803.2:c.1606+294G>A

Benign

Met criteria codes 2

BS3_Supporting BA1

Not Met criteria codes 24

BS2 BS1 BS4 BP4 BP3 BP1
BP2 BP5 BP7 PS1 PS2 PS3

Expert Panel

Familial Hypercholesterolemia VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

PS4 PP1 PP2 PP3 PP4
PM1 PM3 PM5 PM4 PM6
PM2 PVS1

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

NM_000527.5(LDLR):c.2140+5G>A variant is classified as Benign for Familial Hypercholesterolemia by applying evidence codes (BA1, BS3_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: BA1 - FAF = 0.01030 (1.030%) in European non-Finnish exomes (gnomAD v2.1.1). BS3_supporting - Level 3 assay: PMID:19208450 - study on patient's lymphocytes, Northern blot + real-time PCR + FACS used: normal mRNA processing + 108% low-density lipoprotein receptor activity. ---- functional study is consistent with no damaging effect.

Met criteria codes

BS3_Supporting	✓	Level 3 assay: PMID:19208450 - study on patient's lymphocytes, Northern blot + real-time PCR + FACS used: normal mRNA processing + 108% low-density lipoprotein receptor activity. ---- functional study is consistent with no damaging effect.
BA1	✓	FAF = 0.01030 (1.030%) in European non-Finnish exomes (gnomAD v2.1.1). FAF is above 0.5%

Not Met criteria codes

BS2	✗	Most of labs do not track clinical data in this variant due to classifying as benign in the past.
BS1	✗	BA1 is met. Not applicable.
BS4	✗	Most of labs do not track clinical data in this variant due to classifying as benign in the past.
BP4	✗	Functional data available. Not applicable.
BP3	✗	Not applicable.
BP1	✗	Not applicable.
BP2	✗	Most of labs do not track clinical data in this variant due to classifying as benign in the past.
BP5	✗	Not applicable.
BP7	✗	Intronic variant. Not applicable.

PS1	✖	Intronic variant. Not applicable.
PS2	✖	No de novo cases were identified.
PS3	✖	No well established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product.
PS4	✖	PM2 is not met. Not applicable.
PP1	✖	Most of labs do not track clinical data in this variant due to classifying as benign in the past.
PP2	✖	Not applicable.
PP3	✖	Functional data available. Not applicable.
PP4	✖	PM2 is not met. Not applicable.
PM1	✖	Intronic variant. Not applicable.
PM3	✖	Most of labs do not track clinical data in this variant due to classifying as benign in the past.
PM5	✖	Intronic variant. Not applicable.
PM4	✖	Intronic variant. Not applicable.
PM6	✖	No de novo cases were identified.
PM2	✖	PopMax MAF = 0.03088 (3.1%) in Ashkenazi Jewish exomes (gnomAD v2.1.1). FAF is not below 0.02%.
PVS1	✖	Intronic variant outside the canonical +/- 1 or 2 splice sites. Not applicable.

Curation History

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ee Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000527.5(LDLR):c.2140+5G>A	Benign	Hypercholesterolemia, Familial	2021-06-24	1.0	-	LDLR

owing 1 to 1 of 1 rows
