

Variant: NM_000527.5(LDLR):c.1845G>A (p.Glu615=)

Version: 1.0

CA500025 [↗](#)

252065 (ClinVar) [↗](#)

Gene: LDLR ([HGNC:3949](#))

Condition: hypercholesterolemia, familial ([MONDO:0007750](#))

Inheritance Mode: Semidominant inheritance

UUID: a90b351c-b5af-4371-9975-29978dc4247e

Approved on: 2022/8/29

Published on: 2022/12/23

HGVS expressions

NM_000527.5:c.1845G>A

NM_000527.5(LDLR):c.1845G>A (p.Glu615=)

NC_000019.10:g.11116998G>A

CM000681.2:g.11116998G>A

NC_000019.9:g.11227674G>A

CM000681.1:g.11227674G>A

NC_000019.8:g.11088674G>A

NG_009060.1:g.32618G>A

ENST00000252444.10:c.2103G>A

ENST00000559340.2:c.1705+786G>A

ENST00000560467.2:c.1725G>A

ENST00000558518.6:c.1845G>A

ENST00000252444.9:c.2099G>A

ENST00000455727.6:c.1341G>A

ENST00000535915.5:c.1722G>A

ENST00000545707.5:c.1464G>A

ENST00000557933.5:c.1845G>A

ENST00000558013.5:c.1845G>A

ENST00000558518.5:c.1845G>A

ENST00000559340.1:c.426+786G>A

NM_000527.4:c.1845G>A

NM_001195798.1:c.1845G>A

NM_001195799.1:c.1722G>A

NM_001195800.1:c.1341G>A

NM_001195803.1:c.1464G>A

NM_001195798.2:c.1845G>A

NM_001195799.2:c.1722G>A

NM_001195800.2:c.1341G>A

NM_001195803.2:c.1464G>A

Uncertain Significance

Met criteria codes **3**

PM2

PP3

PP4

Not Met criteria codes **8**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1845G>A (p.Glu615=) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes PM2, 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: The only >10,000 subpopulation is European (Non-Finnish), in which the variant is absent. So PM2 is met. PP3: No REVEL, splicing evaluation required. Functional data on splicing not available. A) variant located -3 to +6 from canonical donor site MES scores: canonical site variant = -1.8; canonical donor wt = 4.48. Ratio: -1.8/4.48 = -0.4 ---- It is below 0.8. Variant is predicted to alter splicing. So PP3 is met. PP4: Variant meets PM2 and is identified in 1 case fulfilling Simon-Broome criteria for possible FH published in PMID: 17539906 (Taylor et al., 2007). So PP4 is met.

Met criteria codes

PM2			The only >10,000 subpopulation is European (Non-Finnish), in which the variant is absent. So PM2 is met.
PP3			No REVEL, splicing evaluation required. Functional data on splicing not available. A) variant located -3 to +6 from canonical donor site MES scores: canonical site variant = -1.8; canonical donor wt = 4.48. Ratio: -1.8/4.48 = -0.4 ---- It is below 0.8. Variant is predicted to alter splicing. So PP3 is met.
PP4			Variant meets PM2 and is identified in 1 case fulfilling Simon-Broome criteria for possible FH published in PMID: 17539906 (Taylor et al., 2007). So PP4 is met.

Not Met criteria codes

PM4			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
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			Not a null variant
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP4			No REVEL, splicing evaluation required. Functional data on splicing not available. A) variant located -3 to +6 from canonical donor site MES scores: canonical site variant = -1.8; canonical donor wt = 4.48. Ratio: $-1.8/4.48 = -0.4$ ---- It is below 0.8. Variant is predicted to alter splicing.
BP3			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

Curation History 	
   owing 1 to 1 of 1 rows	

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