

Variant: NM_000527.5(LDLR):c.2113G>C (p.Ala705Pro)

Version: 1.0

CA023637 [↗](#)

36459 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: cc00e79a-6117-45c6-a00e-c5726b9419c4

Approved on: 2022/2/11

Published on: 2022/4/25

HGVS expressions

NM_000527.5(LDLR):c.2113G>C (p.Ala705Pro)

NM_000527.5:c.2113G>C

NC_000019.10:g.11120495G>C

CM000681.2:g.11120495G>C

NC_000019.9:g.11231171G>C

CM000681.1:g.11231171G>C

NC_000019.8:g.11092171G>C

NG_009060.1:g.36115G>C

ENST00000252444.10:c.2371G>C

ENST00000559340.2:c.*182G>C

ENST00000560467.2:c.1993G>C

ENST00000558518.6:c.2113G>C

ENST00000252444.9:c.2367G>C

ENST00000455727.6:c.1609G>C

ENST00000535915.5:c.1990G>C

ENST00000545707.5:c.1606+262G>C

ENST00000557933.5:c.2113G>C

ENST00000558013.5:c.2113G>C

ENST00000558518.5:c.2113G>C

NM_000527.4:c.2113G>C

NM_001195798.1:c.2113G>C

NM_001195799.1:c.1990G>C

NM_001195800.1:c.1609G>C

NM_001195803.1:c.1606+262G>C

NM_001195798.2:c.2113G>C

NM_001195799.2:c.1990G>C

NM_001195800.2:c.1609G>C

NM_001195803.2:c.1606+262G>C

Uncertain Significance

Met criteria codes **3**

PP3 PP4 PM2

Not Met criteria codes **2**

PS3 PM5

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5 (LDLR): c.2113G>C (p.Ala705Pro) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying evidence codes (PM2, PP4, PP3) 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 Met: PopMAX MAF = 0.00001 in European (Non-Finnish) population in gnomAD (gnomAD v2.1.1). PP4 Met: This variant meets PM2 and is identified in 1 index case who met clinical criteria for FH after alternative causes for high cholesterol were excluded (Department of Vascular Medicine, Academic Medical Center at the University of Amsterdam, Amsterdam, The Netherlands, PMID 11810272). PP3 Met: REVEL score = 0.78, which is above the threshold of 0.75. PS3 not met: There is no functional experiment reported for this variant. PM5 not met: There is one other variant in the same codon: LDLR: NM_000527:c.2113G>T (p.Ala705Ser) is classified as Uncertain significance - insufficient evidence by these guidelines. Therefore PM5 is not met.

Met criteria codes

PP3			REVEL score = 0.78, which is above the threshold of 0.75.
PP4			This variant meets PM2 and is identified in 1 index case who met clinical criteria for FH after alternative causes for high cholesterol were excluded (Department of Vascular Medicine, Academic Medical Center at the University of Amsterdam, Amsterdam, The Netherlands, PMID 11810272).
PM2			PopMAX MAF = 0.00001 in European (Non-Finnish) population in gnomAD (gnomAD v2.1.1).

Not Met criteria codes

PS3			There is no functional experiment reported for this variant.
PM5			There is one other variant in the same codon: LDLR: NM_000527:c.2113G>T (p.Ala705Ser) is classified as Uncertain significance - insufficient evidence by these guidelines. Therefore PM5 is not met.

Curation History

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The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.