

Variant: NM_000527.5(LDLR):c.1987+10G>T

CA037694 [↗](#)

252149 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: cf7b231e-0673-441b-a83b-170433c8ce09

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HGVS expressions

NM_000527.5(LDLR):c.1987+10G>T

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NC_000019.10:g.11120243G>T

CM000681.2:g.11120243G>T

NC_000019.9:g.11230919G>T

CM000681.1:g.11230919G>T

NC_000019.8:g.11091919G>T

NG_009060.1:g.35863G>T

ENST00000252444.10:c.2245+10G>T

ENST00000559340.2:c.*56+10G>T

ENST00000560467.2:c.1867+10G>T

ENST00000558518.6:c.1987+10G>T

ENST00000252444.9:c.2241+10G>T

ENST00000455727.6:c.1483+10G>T

ENST00000535915.5:c.1864+10G>T

ENST00000545707.5:c.1606+10G>T

ENST00000557933.5:c.1987+10G>T

ENST00000558013.5:c.1987+10G>T

ENST00000558518.5:c.1987+10G>T

ENST00000559340.1:c.568+10G>T

NM_000527.4:c.1987+10G>T

NM_001195798.1:c.1987+10G>T

NM_001195799.1:c.1864+10G>T

NM_001195800.1:c.1483+10G>T

NM_001195803.1:c.1606+10G>T

NM_001195798.2:c.1987+10G>T

NM_001195799.2:c.1864+10G>T

NM_001195800.2:c.1483+10G>T

NM_001195803.2:c.1606+10G>T

Uncertain Significance

Met criteria codes **4**

PM2 BP4 PP4 PS4_Supporting

Not Met criteria codes **14**

PM4 BA1 BS4 BS3 BS1
PVS1 BS2 BP7 BP3 BP1

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1987+10G>T variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PP4, PS4_Supporting and BP4 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 24 March 2025. The supporting evidence is as follows: PM2: PopMax MAF = 0.00008220 (0.00822%) in Non-Finnish European (gnomAD v4.1.0). PS4_Supporting, PP4: Variant meets PM2 and is identified in 2 unrelated cases who fulfill Simon Broome criteria for possible FH from Centre de Génétique Moléculaire et Chromosomique, Unité de génétique de l'Obésité et des Dyslipidémies, APHP.Sorbonne Université, Hôpital de la Pitié-Salpêtrière, France. BP4: No REVEL, splicing evaluation required. SpliceAI: acceptor loss = 0.01, donor loss = 0.04. Variant is not predicted to alter splicing.

Met criteria codes

PM2			PopMax MAF = 0.0000822 (0.00822%) in European (non-Finnish) (gnomAD v4.0). PM2 is met since PopMax MAF<0.02%
BP4			No REVEL, splicing evaluation required. Functional data on splicing not available, the variante not on limits. Variant outside the limits considered to alter splicing, and therefore BP4 is considered as met. (SlippeAI results - Acceptor Loss 0.01 and Donor Loss 0.04)
PP4			Variant meets PM2 and is identified in at least 1 index case fulfilling FH criteria (SB possible), after alternative causes of high cholesterol were excluded, from Centre de Génétique Moléculaire et Chromosomique, Unité de génétique de l'Obésité et des Dyslipidémies (APHP.Sorbonne Université, Hôpital de la Pitié-Salpêtrière)
PS4_Supporting			Variant meets PM2 and is identified in at least 2 index cases who fulfill criteria for FH (SB possible), after alternative causes of high cholesterol were excluded: 2 index cases Centre de Génétique Moléculaire et Chromosomique, Unité de génétique de l'Obésité et des Dyslipidémies (APHP.Sorbonne Université, Hôpital de la Pitié-Salpêtrière)

Not Met criteria codes

PM4			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
BS4			not met, (no information of index cases or report of segregation data/cases).

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