

## Variant: *NM\_000527.5(LDLR):c.2479G>T (p.Val827Phe)*

Version: 1.1

[CA16602353](#) 

[375840 \(ClinVar\)](#) 

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

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

**Inheritance Mode:** Semidominant inheritance

**UUID:** ad250858-bb45-464e-a96e-b94160859000

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### *HGVS expressions*

#### **NM\_000527.5:c.2479G>T**

NM\_000527.5(LDLR):c.2479G>T (p.Val827Phe)

NC\_000019.10:g.11129602G>T

CM000681.2:g.11129602G>T

NC\_000019.9:g.11240278G>T

CM000681.1:g.11240278G>T

NC\_000019.8:g.11101278G>T

NG\_009060.1:g.45222G>T

ENST00000252444.10:c.2737G>T

ENST00000559340.2:c.\*548G>T

ENST00000560467.2:c.2359G>T

ENST00000558518.6:c.2479G>T

ENST00000252444.9:c.2733G>T

ENST00000455727.6:c.1975G>T

ENST00000535915.5:c.2356G>T

ENST00000545707.5:c.1945G>T

ENST00000557933.5:c.2541G>T

ENST00000558013.5:c.2479G>T

ENST00000558518.5:c.2479G>T

ENST00000560628.1:n.108+1948G>T

NM\_000527.4:c.2479G>T

NM\_001195798.1:c.2479G>T

NM\_001195799.1:c.2356G>T

NM\_001195800.1:c.1975G>T

NM\_001195803.1:c.1945G>T

NM\_001195798.2:c.2479G>T

NM\_001195799.2:c.2356G>T

NM\_001195800.2:c.1975G>T

NM\_001195803.2:c.1945G>T

Uncertain Significance

Met criteria codes **2**

PP3 PM2

Not Met criteria codes **24**

Expert Panel

Familial Hypercholesterolemia VCEP 

Criteria Specification Information

[PVS1](#) [BA1](#) [BP4](#) [BP3](#) [BP1](#)  
[BP2](#) [BP5](#) [BP7](#) [BS2](#) [BS1](#) [BS4](#)  
[BS3](#) [PP1](#) [PP2](#) [PP4](#) [PS1](#) [PS2](#)  
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[Criteria Specification: ClinGen Familial Hypercholesterolemia Expert Panel Specifications to the ACMG/AMP Variant Classification Guidelines Version 1.1](#)  
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Evidence submitted by expert panel

















**Familial Hypercholesterolemia VCEP**































The NM\_000527.5(LDLR):c.2479G>T (p.Val827Phe) variant is classified as **Uncertain significance - insufficient evidence for Familial Hypercholesterolemia** by applying evidence codes **PM2** and **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** - This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is met. **PP3** - REVEL = 0.86. It is above 0.75, so PP3 is met

**Met criteria codes**

- |            |   |   |  |
|------------|---|---|--|
| <b>PP3</b> |  |  | REVEL = 0.86. It is above 0.75, so PP3 is met                      |
| <b>PM2</b> |  |  | This variant is absent from gnomAD (gnomAD v2.1.1), so PM2 is met. |

**Not Met criteria codes**

- |             |   |   |  |
|-------------|---|---|--|
| <b>PVS1</b> |  |  | variant is missense and not in initiation codon, so not met    |
| <b>BA1</b>  |  |  | This variant is absent from gnomAD (gnomAD v2.1.1), so not met |
| <b>BP4</b>  |  |  | REVEL = 0.86. It is not below 0.50, so BP4 is not met          |
| <b>BP3</b>  |  |  | not applicable   |
| <b>BP1</b>  |  |  | not applicable   |
| <b>BP2</b>  |  |  | there is no case data  |
| <b>BP5</b>  |  |  | not applicable   |
| <b>BP7</b>  |  |  | variant is missense, so not met                                |
| <b>BS2</b>  |  |  | there is no case data  |

<b>BS1</b>			This variant is absent from gnomAD (gnomAD v2.1.1), so not met
<b>BS4</b>			there is no case data
<b>BS3</b>			there are no published functional studies for this variant
<b>PP1</b>			there is no case data
<b>PP2</b>			not applicable
<b>PP4</b>			there is no case data
<b>PS1</b>			no other variant leads to the same amino acid change, so not met
<b>PS2</b>			there is no case data
<b>PS3</b>			there are no published functional studies for this variant
<b>PS4</b>			there is no case data
<b>PM1</b>			variant is missense and meets PM2, but is not in exon 4 and does not alter Cys, so not met
<b>PM3</b>			there is no case data
<b>PM5</b>			2 more missense variants in same codon: (1) NM_000527.5(LDLR):c.2479G>A (p.Val827Ile) - 3 stars, VUS by these guidelines (FH VCEP) in ClinVar (2) NM_000527.5(LDLR):c.2480T>A (p.Val827Asp) - 1 star, VUS in ClinVar - VUS by these guidelines no Pathogenic by these guidelines, so not met
<b>PM4</b>			variant is missense, so not met
<b>PM6</b>			there is no case data

Curation History [↗](#)

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