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Variant: NM_000432.4(MYL2):c.485G>A (p.Gly162Glu)

Version: 1.0

CA010439

43479 (ClinVar)

Gene: MYL2 (HGNC:4633)
Condition: hypertrophic cardiomyopathy (MONDO:0005045)
Inheritance Mode: Autosomal dominant inheritance
UUID: 13402a8e-742a-4ab7-a80f-b053d6263f8d
Approved on: 2025/11/14
Published on: 2025/11/14

HGVS expressions

NM_000432.4:c.485G>A
NM_000432.4(MYL2):c.485G>A (p.Gly162Glu)
NC_000012.12:g.110911093C>T
CM000674.2:g.110911093C>T
NC_000012.11:g.111348897C>T
CM000674.1:g.111348897C>T
NC_000012.10:g.109833280C>T
NG_007554.1:g.14485G>A
ENST00000228841.15:c.485G>A
ENST00000663220.1:c.428G>A
ENST00000228841.12:c.485G>A
ENST00000548438.1:c.443G>A
NM_000432.3:c.485G>A

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PS4_Supporting PP1_Strong

Not Met criteria codes 9

BA1 PM6 PM5 BS1 BS3 PS1 PS2 PS3 BP4

Evidence Links 0

Expert Panel

Cardiomyopathy VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Cardiomyopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYL2 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Cardiomyopathy VCEP

NM_000432.4(MYL2):c.485G>A (p.Gly162Glu). This variant has been identified in individuals with HCM and other cardiomyopathies (ClinVar Variation ID 164114) and segregated with disease in 11 affected relatives from one family (PP1_Strong; Renaudin 2018 PMID: 29549657). It was absent from large population studies (PM2_Supporting; https://gnomad.broadinstitute.org/; v.2.1). The variant is statistically increased in individuals with HCM compared to controls (OR lower 95% CI>5), therefore, the PS4 criterion has been applied at supporting strength (PS4_Supporting). Computational prediction tools and conservation analyses suggest that this variant may impact the protein

(PP3; REVEL score ≥0.70). In summary, this variant meets criteria to be classified as likely pathogenic for hypertrophic cardiomyopathy in an autosomal dominant manner based on PS4_Supporting, PM2_Supporting, PP1_Strong, PP3.

Met criteria codes

PM2_Supporting	✔	Absent from gnomAD 2.1 and 4.1.0
PP3	✔	Computational prediction tools and conservation analyses suggest that this variant may impact the protein (PP3; REVEL score ≥0.70)
PS4_Supporting	✔	Walsh 2017 - 3/2650 LMM Gnomad 2.1 - absent (NFE denominator as variant in same codon 112196) 3 in 2650 case genotypes vs 1 in 56098 control genotypes gives an odds ratio of 63.58 (95%CI=6.61-611.41) Lower bound CI: Strong 95%CI=6.61 (threshold for strong ≥20) Moderate 95%CI=6.61 (threshold for moderate ≥10) Supporting 95%CI=6.61 (threshold for supporting ≥5) The lower bound 95%CI is greater than 5 (95%CI=6.61). Therefore PS4 is set to PS4_Supporting
PP1_Strong	✔	Renaudin - 1 HCM and 11 segregations

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	NM_000432.4(MYL2):c.484G>A (p.Gly162Arg) - is VUS
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	✖	no studies
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	✖	no studies
BP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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