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Variant: NM_000257.4(MYH7):c.1207C>T (p.Arg403Trp)

CA010360

14102 (ClinVar)

Gene: MYH7 (HGNC:4625)
Condition: hypertrophic cardiomyopathy (MONDO:0005045)
Inheritance Mode: Autosomal dominant inheritance
UUID: d065fb29-95bd-49a8-951e-f52b10fac57c
Approved on: 2016-12-15
Published on: 2018-11-16

HGVS expressions

NM_000257.4(MYH7):c.1207C>T (p.Arg403Trp)
NM_000257.4:c.1207C>T
NC_000014.9:g.23429279G>A
CM000676.2:g.23429279G>A
NC_000014.8:g.23898488G>A
CM000676.1:g.23898488G>A
NC_000014.7:g.22968328G>A
NG_007884.1:g.11383C>T
ENST00000355349.4:c.1207C>T
ENST00000355349.3:c.1207C>T
NM_000257.3:c.1207C>T

Pathogenic

Met criteria codes 6

PP1_Strong PS4 PP3 PM1 PM5 PM2

Evidence Links 4

Expert Panel

Cardiomyopathy VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Cardiomyopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYH7 Version 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Cardiomyopathy VCEP

The c.1207C>T (p.Arg403Trp) variant in MYH7 has been reported in >20 individuals with hypertrophic cardiomyopathy and segregated with disease in >20 affected family members (PS4 and PP1_Strong; PMID:1052196; PMID:7662452; PMID:7848420; PMID:8254035; PMID:8268932; PMID:12707239; PMID:12974739; PMID:15010274; PMID:15856146; PMID:17612745; PMID:20428263; PMID:21239446; PMID:26383716; Partners LMM ClinVar SCV000059358.5; AGCMC Sydney ClinVar SCV000212643.1; SHaRe consortium, PMID: 30297972). This variant was absent from large population studies (PM2; http://exac.broadinstitute.org). This variant lies in the head region of the protein (aa 181-937) and missense variants in this region are statistically more likely to be disease-associated (PM1; PMID:27532257). Computational prediction tools and conservation analysis suggest that this variant may impact the protein (PP3). A different pathogenic missense variant has been previously identified at this codon which may indicate that this residue is critical to the function of the protein

(PM5; c.1208G>A p.Arg403Gln - Variation ID 14087). In summary, this variant meets criteria to be classified as pathogenic for hypertrophic cardiomyopathy in an autosomal dominant manner. MYH7-specific ACMG/AMP criteria applied (PMID:29300372): PS4; PP1_Strong; PM1; PM2; PM5; PP3

Met criteria codes

PP1_Strong	✔	>20 segregations Variant segregated with disease in 11 family members PubMed:17612745 Variant segregated with disease in 5 affected family members PubMed:8254035 Variant segregated with disease in 12 family members PubMed:7662452
PS4	✔	>20 probands with HCM reported
PP3	✔	Tools suggest damaging
PM1	✔	Variants in head region of the protein (aa 181-937) are statistically more likely to be disease-associated Variants in head region of the protein (aa 181-937) are statistically more likely to be disease-associated PubMed:27532257
PM5	✔	c.1208G>A (p.Arg403Gln) - Variation ID 14087 - Pathogenic by ClinGen Expert Panel
PM2	✔	Absent from ExAC

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000257.4(MYH7):c.1207C>T (p.Arg...	Pathogenic	Hypertrophic Cardiomyopathy	2026-06-04	1.1	ClinGen Cardiomyopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYH7 Version 2.0.0	MYH7
View	NM_000257.3(MYH7):c.1207C>T (p.Arg...	Pathogenic	Hypertrophic Cardiomyopathy	2018-11-16	1.0	-	MYH7

Showing 1 to 2 of 2 rows

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