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Variant: NM_030662.3(MAP2K2):c.169T>G (p.Phe57Val)

Version: 1.0

CA279960

8273 (ClinVar)

Gene: MAP2K2 (HGNC:5605)
Condition: cardiofaciocutaneous syndrome (MONDO:0015280)
Inheritance Mode: Autosomal dominant inheritance
UUID: ac054f0f-9da0-455d-8a0f-343d2f4ad540
Approved on: 2017/5/9
Published on: 2019/7/15

HGVS expressions

NM_030662.3(MAP2K2):c.169T>G (p.Phe57Val)
NM_030662.3:c.169T>G
NC_000019.10:g.4117553A>C
CM000681.2:g.4117553A>C
NC_000019.9:g.4117551A>C
CM000681.1:g.4117551A>C
NC_000019.8:g.4068551A>C
NG_007996.1:g.11576T>G
ENST00000394867.9:n.608T>G
ENST00000687128.1:n.608T>G
ENST00000262948.10:c.169T>G
ENST00000262948.9:c.169T>G
ENST00000394867.8:c.-123T>G
ENST00000599345.1:n.366T>G
NM_030662.4:c.169T>G

Pathogenic

Met criteria codes 5

PP2 PP3 PS2_Very Strong PM1 PM2

Evidence Links 1

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.169T>G (p.Phe57Val) variant in MAP2K2 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VeryStrong; PMID 18042262). The variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of MAP2K2 (PM1; PMID 29493581). This variant was absent from large population studies (PM2; ExAC, http://exac.broadinstitute.org). The variant is located in the MAP2K2 gene, which has been defined by the ClinGen RASopathy Expert Panel as a gene with a low rate of benign missense variants and pathogenic missense variants are common (PP2; PMID: 29493581). Computational prediction tools and conservation analysis suggest that the p.Phe57Val variant may impact the protein (PP3). In

summary, this variant meets criteria to be classified as pathogenic for RASopathies in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): PS2_VeryStrong, PM1, PM2, PP2, PP3.

Met criteria codes

PP2	✔	The variant is located in the MAP2K2 gene, which has been defined by the ClinGen RASopathy Expert Panel as a gene with a low rate of benign missense variants and pathogenic missense variants are common (PP2; PMID: 29493581).
PP3	✔	Computational prediction tools and conservation analysis suggest that the p.Phe57Val variant may impact the protein (PP3).
PS2_Very Strong	✔	The c.169T>G (p.Phe57Val) variant in MAP2K2 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VeryStrong; PMID 18042262). 2 patients were identified with confirmed de novo occurrences of the p.Phe57Val PubMed:18042262
PM1	✔	The variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of MAP2K2 (PM1; PMID 29493581).
PM2	✔	This variant was absent from large population studies (PM2; ExAC, http://exac.broadinstitute.org).

Curation History

owing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_030662.3(MAP2K2):c.169T>G (p.P...	Pathogenic	Cardiofaciocutaneous Syndrome	2019-07-15	1.0	-	MAP2K2

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