

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

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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 PM2 PM1 PS2_Very

Strong

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).
PM2			This variant was absent from large population studies (PM2; ExAC, http://exac.broadinstitute.org).
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).
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 

Curation History



 

 

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