

Variant: *NM_002755.3(MAP2K1):c.199G>A (p.Asp67Asn)*

CA180743 [↗](#)

40781 (ClinVar) [↗](#)

Gene: MAP2K1 ([HGNC:5604](#))

Condition: cardiofaciocutaneous syndrome ([MONDO:0015280](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 8197dee3-bc2e-49dc-88bc-d31b5fd7286f

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HGVS expressions

NM_002755.3(MAP2K1):c.199G>A (p.Asp67Asn)

NM_002755.3:c.199G>A

NC_000015.10:g.66435145G>A

CM000677.2:g.66435145G>A

NC_000015.9:g.66727483G>A

CM000677.1:g.66727483G>A

NC_000015.8:g.64514537G>A

NG_008305.1:g.53273G>A

ENST00000307102.9:c.199G>A

ENST00000425818.2:n.710G>A

Pathogenic

Met criteria codes **5**

PM6_Strong

PS3

PP3

PP2

PM2

Evidence Links **2**

Expert Panel

[RASopathy VCEP](#) [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

RASopathy VCEP

The c.199G>A (p.Asp67Asn) variant in MAP2K1 has been reported in the literature in at least 2 unconfirmed de novo occurrences in patients with clinical features of a RASopathy (PM6_Strong; PMID 17704260). In vitro functional studies provide some evidence that the p.Asp67Asn variant may impact protein function (PS3; PMID 25049390). This variant was absent from large population studies (PM2; ExAC, <http://exac.broadinstitute.org>). The variant is located in the MAP2K1 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.Asp67Asn 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): PM6_Strong, PS3, PM2, PP2, PP3.

Met criteria codes

PM6_Strong



			The p.Asp67Asn variant in MAP2K1 has been reported in the literature in at least 2 unconfirmed de novo occurrences in patients with clinical features of a RASopathy (PM6_S; PMID 17704260). The p.Asp67Asn variant in MAP2K1 has been reported in the literature in at least 2 unconfirmed de novo occurrences in patients with clinical features of a RASopathy (PM6_S; PMID 17704260). PubMed:17704260 
PS3			In vitro functional studies provide some evidence that the p.Asp67Asn variant may impact protein function (PS3; PMID 25049390). In vitro functional studies provide some evidence that the p.Asp67Asn variant may impact protein function (PS3; PMID 25049390). PubMed:25049390 
PP3			Computational prediction tools and conservation analysis suggest that the p.Asp67Asn variant may impact the protein (PP3).
PP2			The variant is located in the MAP2K1 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).
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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