The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_002755.3(MAP2K1):c.389A>G (p.Tyr130Cys)

CA280036

13351 (ClinVar)

Gene: MAP2K1 (HGNC:5604)
Condition: cardiofaciocutaneous syndrome (MONDO:0015280)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1eaf4dad-ab0c-49ae-8548-22bad4210249
Approved on: 2017-05-09
Published on: 2018-12-10

HGVS expressions

NM_002755.3(MAP2K1):c.389A>G (p.Tyr130Cys)
NM_002755.3:c.389A>G
ENST00000307102.9:c.389A>G
ENST00000425818.2:n.900A>G
NC_000015.10:g.66436843A>G
CM000677.2:g.66436843A>G
NC_000015.9:g.66729181A>G
CM000677.1:g.66729181A>G
NC_000015.8:g.64516235A>G
NG_008305.1:g.54971A>G

Pathogenic

Met criteria codes 6

PS3 PP3 PP2 PS2_Very Strong PM1 PM2

Evidence Links 6

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.389A>G (p.Tyr130Cys) variant in MAP2K1 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VeryStong; PMID 16439621, 17551924, 18042262). In vitro functional studies provide some evidence that the p.Tyr130Cys variant may impact protein function (PS3; PMID 18413255, 23093928, 17981815). 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). Furthermore, the variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of MAP2K1 (PM1; PMID 29493581). Computational prediction tools and conservation analysis suggest that the p.Tyr130Cys 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, PP3, PS3, PM2, PP2, PM1.

Met criteria codes

PS3	✔	In vitro functional studies provide some evidence that the p.Tyr130Cys variant may impact protein function (PS3; PMID 18413255, 23093928, 17981815). In vitro functional studies provide some evidence that the p.Tyr130Cys variant may impact protein function (PS3; PMID 18413255, 23093928, 17981815). PubMed:18413255 In vitro functional studies provide some evidence that the p.Tyr130Cys variant may impact protein function (PS3; PMID 18413255, 23093928, 17981815). PubMed:17981815 In vitro functional studies provide some evidence that the p.Tyr130Cys variant may impact protein function (PS3; PMID 18413255, 23093928, 17981815). PubMed:23093928
PP3	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2	✔	The variant is in MAP2K1, which has been defined by the ClinGen RASopathy Expert Panel as a gene with low rate of benign missense with missense variants commonly being pathogenic (PP2; PMID 29493581)
PS2_Very Strong	✔	The p.Tyr130Cys variant in MAP2K1 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VS; PMID 16439621, 17551924, 18042262). The p.Tyr130Cys variant in MAP2K1 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VS; PMID 16439621, 17551924, 18042262). PubMed:16439621 The p.Tyr130Cys variant in MAP2K1 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VS; PMID 16439621, 17551924, 18042262). PubMed:18042262 The p.Tyr130Cys variant in MAP2K1 has been reported as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2_VS; PMID 16439621, 17551924, 18042262). PubMed:17551924
PM1	✔	Furthermore, the variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of MAP2K1 (PM1; PMID 29493581)
PM2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



howing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_002755.3(MAP2K1):c.389A>G (p.T...	Pathogenic	Cardiofaciocutaneous Syndrome	2018-12-10	1.0	-	MAP2K1

howing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.

¤ Powered by BCM's Genboree.