Variant: NM_030662.3(MAP2K2):c.619G>A (p.Glu207Lys)

Version: 1.0

CA180944

40813 (ClinVar)

Gene: MAP2K2 (HGNC:5605)
Condition: cardiofaciocutaneous syndrome (MONDO:0015280)
Inheritance Mode: Autosomal dominant inheritance
UUID: 93491eab-4df5-480a-a62b-7022611f18ee
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HGVS expressions

NM_030662.3:c.619G>A
NM_030662.3(MAP2K2):c.619G>A (p.Glu207Lys)
NC_000019.10:g.4101105C>T
CM000681.2:g.4101105C>T
NC_000019.9:g.4101103C>T
CM000681.1:g.4101103C>T
NC_000019.8:g.4052103C>T
NG_007996.1:g.28024G>A
ENST00000394867.9:n.1058G>A
ENST00000687128.1:n.1058G>A
ENST00000689792.1:n.559G>A
ENST00000262948.10:c.619G>A
ENST00000262948.9:c.619G>A
ENST00000394867.8:c.328G>A
ENST00000593364.5:n.566G>A
ENST00000597008.5:n.220G>A
ENST00000597263.5:n.83G>A
ENST00000599345.1:n.889G>A
ENST00000601786.5:n.920G>A
ENST00000602167.5:n.339G>A
NM_030662.4:c.619G>A

Pathogenic

Met criteria codes 5

PS2 PS4 PP2 PM6 PM2

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.619G>A (p.Glu207Lys) variant in MAP2K2 was absent from large population studies (PM2; gnomAD.broadinstitute.org). It has been identified in 6 individuals with clinical features of a RASopathy (PS4; SCV000204213.4, SCV000207959.10, SCV000815593.1, Otto von Guericke University Magdeburg internal data). One of these cases was a confirmed de novo occurrence and another was an unconfirmed de novo occurrence (PS2; PM6; SCV000815593.1, Otto von Guericke University Magdeburg internal data). Additionally, the c.619G>A (p.Glu207Lys) is located in MAP2K2, 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). 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): PS4, PS2, PM6, PM2, PP2.

Met criteria codes

PS2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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).
PM6	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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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