

Variant: *NM_030662.3(MAP2K2):c.842G>A (p.Arg281Gln)*

Version: 1.0

CA403385475 [↗](#)

569590 (ClinVar) [↗](#)

Gene: MAP2K2 ([HGNC:5605](#))

Condition: RASopathy ([MONDO:0021060](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: dfec0bf2-cccf-4932-8cf2-6dabf182615f

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HGVS expressions

NM_030662.3:c.842G>A

NM_030662.3(MAP2K2):c.842G>A (p.Arg281Gln)

NC_000019.10:g.4099278C>T

CM000681.2:g.4099278C>T

NC_000019.9:g.4099276C>T

CM000681.1:g.4099276C>T

NC_000019.8:g.4050276C>T

NG_007996.1:g.29851G>A

ENST00000394867.9:n.1281G>A

ENST00000687128.1:n.1281G>A

ENST00000688002.1:n.1136G>A

ENST00000689792.1:n.746G>A

ENST00000262948.10:c.842G>A

ENST00000262948.9:c.842G>A

ENST00000394867.8:c.551G>A

ENST00000593364.5:n.789G>A

ENST00000595715.1:n.657G>A

ENST00000597263.5:n.169+1741G>A

ENST00000599021.1:c.29+1741G>A

ENST00000600584.5:n.1402G>A

ENST00000601786.5:n.1143G>A

NM_030662.4:c.842G>A

Uncertain Significance

Met criteria codes **2**

BP4

PP2

Not Met criteria codes **4**

PM2

PM1

PM5

BS2

Evidence Links **0**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.842G>A (p.Arg281Gln) variant in MAP2K2 was present in 0.007324% (1/13654) of Latino chromosomes in gnomAD v3. It was observed in one healthy adult male who did not have features of a RASopathy (BS2 not met; Baylor internal data). 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 variants are common (PP2; PMID: 29493581). Computational analysis and splice site predictors suggest that this variant does not impact the protein (BP4). In summary, the clinical significance of this variant is uncertain. RASopathy-specific ACMG/AMP criteria applied: PP2, BP4.

Met criteria codes

BP4			REVEL score 0.032. May add a 3' splice site (predicted by SpliceSiteFinder-like and MaxEntScan but not NNSPLICE or GeneSplicer), however impact to splicing is not predicted to align with the GOF mechanism for MAP2K2-associated RASopathy. 1 animal in the UCSC database (guinea pig) has Q at this site.
PP2			MAP2K2 is a missense-constrained gene.

Not Met criteria codes

PM2			Present in 0.007324% (1/13654) of Latino chromosomes in gnomAD v3. Absent from gnomAD v2.1.1.
PM1			Does not occur between aa 47-65 or 128-138.
PM5			Only 1 other variant in this codon, c.841C>T (p.Arg281Trp), has been reported. It was absent from ClinVar and was classified as a VUS by the EP.
BS2			This variant was seen in 3 unaffected individuals (Invitae internal data, SCV000817942.1; Baylor internal data). One case was a juvenile male tested because his father had idiopathic HCM, but the proband was supposedly unaffected and healthy. This case was not counted because the indication for testing was HCM. In 2 other cases, the variant was inherited and the fathers of the probands were noted to be asymptomatic. One proband was suspected to have NS; the other did not have a diagnosis.

Curation History



 

 

Showing 1 to 1 of 1 rows

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