

*Variant: NM\_030662.3(MAP2K2):c.281C>T (p.Ser94Leu)*

CA180967 [↗](#)

40786 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 2ae26f96-8b07-456f-9375-37c36e0c6d97

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### *HGVS expressions*

**NM\_030662.3(MAP2K2):c.281C>T (p.Ser94Leu)**

**NM\_030662.3:c.281C>T**

NC\_000019.10:g.4117441G>A

CM000681.2:g.4117441G>A

NC\_000019.9:g.4117439G>A

CM000681.1:g.4117439G>A

NC\_000019.8:g.4068439G>A

NG\_007996.1:g.11688C>T

NM\_030662.4:c.281C>T

ENST00000262948.9:c.281C>T

ENST00000394867.8:c.-11C>T

ENST00000599345.1:n.478C>T

Uncertain Significance

Met criteria codes **2**

PP3 PP2

Not Met criteria codes **2**

BS1 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.281C>T (p.Ser94Leu) variant in MAP2K2 has been identified in 2 independent occurrences in patients with a RASopathy; however, in both cases it was inherited from an apparently unaffected parent (BS2 not met; GeneDx, LMM internal data; ClinVar SCV000204231.4; SCV000207977.8). The p.Ser94Leu variant was present in 0.012% (3/24906) of African alleles in gnomAD (PM2 not met, gnomad.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 this variant may impact protein function (PP3). In summary, the clinical significance of the p.Ser94Leu variant is uncertain. ACMG/AMP criteria applied: PP2, PP3.

Met criteria codes

PP3



Computational prediction tools and conservation analysis suggest that this variant may impact protein function (PP3).

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).

Not Met criteria codes

BS1



The p.Ser94Leu variant was present in 0.012% (3/24906) of African alleles in gnomAD (PM2 not met, gnomad.broadinstitute.org).

BS2



Seen in 2 unaffected parents of 2 different probands (Laboratory for Molecular medicine internal data, ClinVar SCV000204231.4)

Curation History [↗](#)



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