

Variant: NM_030662.4(MAP2K2):c.784G>A (p.Val262Ile)

CA137966 [↗](#)

46242 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 89d53e74-33f3-465b-abde-d4f656802fed

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HGVS expressions

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NM_030662.4:c.784G>A

NC_000019.10:g.4099336C>T

CM000681.2:g.4099336C>T

NC_000019.9:g.4099334C>T

CM000681.1:g.4099334C>T

NC_000019.8:g.4050334C>T

NG_007996.1:g.29793G>A

ENST00000394867.9:n.1223G>A

ENST00000687128.1:n.1223G>A

ENST00000688002.1:n.1078G>A

ENST00000689792.1:n.688G>A

ENST00000262948.10:c.784G>A

ENST00000262948.9:c.784G>A

ENST00000394867.8:c.493G>A

ENST00000593364.5:n.731G>A

ENST00000595715.1:n.599G>A

ENST00000597263.5:n.169+1683G>A

ENST00000599021.1:c.29+1683G>A

ENST00000600584.5:n.1344G>A

ENST00000601786.5:n.1085G>A

NM_030662.3:c.784G>A

Uncertain Significance

Met criteria codes **1**

BP4

Not Met criteria codes **5**

PS4

BA1

PP3

PM2

BS1

Evidence Links **0**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen RASopathy Expert Panel
Specifications to the ACMG/AMP Variant Interpretation
Guidelines for MAP2K2 Version 2.1.0

[↗](#) **Criteria Specification Approval History**

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

RASopathy VCEP

The c.784G>A variant in the MAP2K2 gene is a missense variant predicted to cause substitution of valine by isoleucine at amino acid 262 (p.Val262Ile). The filtering allele frequency in gnomAD v4.1.0 is 0.01543% (201/1178752 alleles) in the European (non-Finnish) population (PM2_Supporting/BS1/BA1 are not met). The computational predictor REVEL gives a score of 0.219, which predicts no impact on protein function (BP4). This variant has been identified in 4 independent occurrences in patients with disparate phenotypes of RASopathy (PS4 not met; GeneDx, LMM internal data; GTR ID's 26957, 21766; SCV000207950.9, SCV000063182.5). In summary, this variant meets criteria to be classified as variant of uncertain significance for autosomal dominant RASopathies based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy Variant Curation Expert Panel: BP4 (Specification Version 2.1, 9/17/2024)

Met criteria codes

BP4			REVEL gives a score of 0.219, which predicts no impact on protein function (BP4).
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Not Met criteria codes

PS4			Identified in 4 independent occurrences in patients with disparate phenotypes (PS4 not met; GeneDx, Laboratory for Molecular Medicine internal data; ClinVar SCV000207950.9; SCV000063182.5).
BA1			The filtering allele frequency in gnomAD v4.1.0 is 0.01543% (201/1178752 alleles) in the European (non-Finnish) population (PM2_Supporting/BS1/BA1 are not met).
PP3			REVEL gives a score of 0.219, which predicts no impact on protein function (BP4).
PM2			The filtering allele frequency in gnomAD v4.1.0 is 0.01543% (201/1178752 alleles) in the European (non-Finnish) population (PM2_Supporting/BS1/BA1 are not met).
BS1			The filtering allele frequency in gnomAD v4.1.0 is 0.01543% (201/1178752 alleles) in the European (non-Finnish) population (PM2_Supporting/BS1/BA1 are not met).

Curation History



 

 

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