

Variant: *NM_030662.3(MAP2K2):c.692G>A (p.Arg231His)*

Version: 1.0

CA9090854 [↗](#)

543999 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 9f74ed62-a0c3-40e1-b0b2-7aa680c29fe2

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HGVS expressions

NM_030662.3(MAP2K2):c.692G>A (p.Arg231His)

NM_030662.3:c.692G>A

NC_000019.10:g.4101032C>T

CM000681.2:g.4101032C>T

NC_000019.9:g.4101030C>T

CM000681.1:g.4101030C>T

NC_000019.8:g.4052030C>T

NG_007996.1:g.28097G>A

ENST00000262948.9:c.692G>A

ENST00000394867.8:c.401G>A

ENST00000593364.5:n.639G>A

ENST00000597008.5:n.293G>A

ENST00000597263.5:n.156G>A

ENST00000599021.1:n.16G>A

ENST00000601786.5:n.993G>A

ENST00000602167.5:n.412G>A

Uncertain Significance

Met criteria codes **2**

PP2 PP3

Not Met criteria codes **21**

PM6 PM2 PM1 PM5 PM4
BS2 BS1 BS4 BS3 PS1 PS2
PS3 PS4 BP4 BP3 BP1 BP2
BP5 BP7 BA1 PP1

Evidence Links **0**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.692G>A (p.Arg231His) variant in MAP2K2 has been identified in a patient with clinical features consistent with cardiomyopathy (PS4 not met; Invitae internal data, GTR Lab ID 500031; ClinVar SCV000776886.1). 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 the p.Arg231His variant may impact the protein (PP3). In summary, the clinical significance of the p.Arg231His variant is uncertain. RASopathy-specific ACMG/AMP criteria applied (PMID:29493581): PP2, PP3.

Met criteria codes

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)
PP3			Computational prediction tools and conservation analysis suggest that the p.Arg231His variant may impact the protein (PP3).

Not Met criteria codes

PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			This variant has been identified in 1/4152 Other alleles in gnomAD. therefore PM2 cannot be applied.
PM1			aa 47-65, 128-138
PM5			p.Arg231Leu variant has also been identiifed, but will not be classified as Pathogenic
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			Variant's frequency in Other alleles is just under BS1 cutoff but only 1 allele so shouldn't be applied.
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4			Invitae: Observed variant in a patient with cardiomyopathy
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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