

Variant: NM_004333.6(BRAF):c.622A>G (p.Ile208Val)

Version: 2.1

CA183392 [↗](#)

178963 (ClinVar) [↗](#)

Gene: BRAF ([HGNC:673](#))

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d9d2d562-8f46-4daf-85e4-fb09d4ba5e5f

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HGVS expressions

NM_004333.6:c.622A>G

NM_004333.6(BRAF):c.622A>G (p.Ile208Val)

NC_000007.14:g.140808049T>C

CM000669.2:g.140808049T>C

NC_000007.13:g.140507849T>C

CM000669.1:g.140507849T>C

NC_000007.12:g.140154318T>C

NG_007873.3:g.121716A>G

ENST00000646891.2:c.622A>G

ENST00000288602.11:c.622A>G

ENST00000496384.7:c.622A>G

ENST00000497784.2:c.*72A>G

ENST00000642228.1:c.622A>G

ENST00000642272.1:n.654A>G

ENST00000642875.1:n.116A>G

ENST00000643356.1:n.223A>G

ENST00000644120.1:n.1064A>G

ENST00000644905.1:n.711A>G

ENST00000644969.2:c.622A>G

ENST00000646730.1:c.622A>G

ENST00000646891.1:c.622A>G

ENST00000288602.10:c.622A>G

ENST00000497784.1:c.657A>G

NM_004333.4:c.622A>G

NM_001354609.1:c.622A>G

NM_004333.5:c.622A>G

NR_148928.1:n.927A>G

NM_001354609.2:c.622A>G

NM_001374244.1:c.622A>G

NM_001374258.1:c.622A>G

NM_001378467.1:c.631A>G

NM_001378468.1:c.622A>G

NM_001378469.1:c.622A>G

NM_001378470.1:c.520A>G

NM_001378471.1:c.622A>G

NM_001378472.1:c.466A>G

NM_001378473.1:c.466A>G

NM_001378474.1:c.622A>G
NM_001378475.1:c.358A>G

Likely Benign

Met criteria codes 2

PP2 BS2

Not Met criteria codes 2

BP4 PP3

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.622A>G (p.Ile208Val) variant in BRAF is present in 0.00001% (2/128934) European alleles in gnomAD. The computational predictor REVEL gives a score of 0.318, which is neither above nor below the thresholds predicting a damaging or benign impact on BRAF function. This variant was observed in two healthy adult individuals who did not have clinical features of a RASopathy (SCV000205449.5; PMID:29945942). Additionally, 12 apparently unaffected parental samples were observed with this variant (BS2; SCV000329576.8, SCV001011557.1). The variant is located in the BRAF 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). In summary, this variant meets the criteria to be classified as likely benign for autosomal dominant RASopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy VCEP: BS2, PP2 (RASopathy VCEP specifications version 1; 8/11/22).

Met criteria codes

PP2			BRAF, in which the variant was identified, is defined by the ClinGen RASopathy VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease (PP2).
BS2			This variant was observed in two healthy adult individuals who did not have clinical features of a RASopathy (SCV000205449.5; PMID:29945942). Additionally, 12 apparently unaffected parental samples were observed with this variant (BS2; SCV000329576.8, SCV001011557.1, PMID:29945942).

Not Met criteria codes

BP4			The computational predictor REVEL gives a score of 0.318, which is neither above nor below the thresholds predicting a damaging or benign impact on BRAF function.
PP3			The computational predictor REVEL gives a score of 0.318, which is neither above nor below the thresholds predicting a damaging or benign impact on BRAF function.











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