

Variant: NM_004333.6(BRAF):c.1024A>G (p.Ile342Val)

Version: 1.1

CA4516829 [↗](#)

359048 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: c21de2c5-2ae3-4535-bcee-ed2d1822a1a7

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HGVS expressions

NM_004333.6(BRAF):c.1024A>G (p.Ile342Val)

NM_004333.6:c.1024A>G

NC_000007.14:g.140794424T>C

CM000669.2:g.140794424T>C

NC_000007.13:g.140494224T>C

CM000669.1:g.140494224T>C

NC_000007.12:g.140140693T>C

NG_007873.3:g.135341A>G

ENST00000646891.2:c.1024A>G

ENST00000288602.11:c.1024A>G

ENST00000496384.7:c.1024A>G

ENST00000497784.2:c.*474A>G

ENST00000642228.1:c.*102A>G

ENST00000642875.1:n.475-9A>G

ENST00000644120.1:n.1423-9A>G

ENST00000644650.1:c.120A>G

ENST00000644905.1:n.1113A>G

ENST00000644969.2:c.1024A>G

ENST00000646730.1:c.1024A>G

ENST00000646891.1:c.1024A>G

ENST00000647434.1:c.67A>G

ENST00000288602.10:c.1024A>G

ENST00000497784.1:c.1059A>G

NM_004333.4:c.1024A>G

NM_001354609.1:c.1024A>G

NM_004333.5:c.1024A>G

NR_148928.1:n.1329A>G

NM_001354609.2:c.1024A>G

NM_001374244.1:c.1024A>G

NM_001374258.1:c.1024A>G

NM_001378467.1:c.1033A>G

NM_001378468.1:c.1024A>G

NM_001378469.1:c.1024A>G

NM_001378470.1:c.922A>G

NM_001378471.1:c.1024A>G

NM_001378472.1:c.868A>G

NM_001378473.1:c.868A>G

NM_001378474.1:c.1024A>G
NM_001378475.1:c.760A>G

Uncertain Significance

Met criteria codes 1

PP2

Not Met criteria codes 5

PP3

PM2

PM1

BS2

BP4

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.1024A>G (p.Ile342Val) variant in BRAF has been identified in 0.005644% (2/35438) of Latino chromosomes in gnomAD v2.1.1. This variant has been observed in several individuals whose clinical presentations lacked clear associations with a RASopathy (Invitae internal data, SCV000820707.1; Fulgent internal data; Baylor internal data; Greenwood Genetic Center internal data). Of note, this variant has also been seen in apparently unaffected parental samples (n=8) evaluated during whole exome sequencing suggesting that this variant may be likely benign; however, these cases were not well-phenotyped and therefore do not meet current requirements for BS2 (BS2 not met; GeneDx internal data, SCV000617143.2). Computational prediction tools and conservation analyses do not provide strong support for pathogenicity given the disease mechanism. In summary, the clinical significance of this variant is uncertain.

Met criteria codes

PP2			BRAF is a missense-constrained gene.
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Not Met criteria codes

PP3			REVEL score 0.269. Alamut indicates that this mutation might shift the 3' splice site upstream by 8 nucleotides. No animals in UCSC have valine at this site.
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PM2			Present in 0.005644% (2/35438) of Latino chromosomes in gnomAD v2; present in 0.007749% (5/64524) of non-Finnish European genomes in gnomAD v3.
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PM1			Does not occur in exon 6, exon 11, aa 459-474, or aa 594-627.
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BS2			GeneDx identified this variant in 8 unaffected parents from 8 different trios, although unclear if they were well phenotyped (SCV000617143.2). However, it was also observed in several individuals whose clinical presentations lacked clear associations with a RASopathy (Invitae internal data, SCV000820707.1; Fulgent internal data; Baylor internal data; Greenwood Genetic Center internal data).
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BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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Curation History



 

 

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