

Variant: NM_004333.4(BRAF):c.1227A>G (p.Ser409=)

CA135058 [↗](#)

40360 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: dd0b96ec-49ad-4f28-801a-b7b31c5fe734

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HGVS expressions

NM_004333.4(BRAF):c.1227A>G (p.Ser409=)

NM_004333.4:c.1227A>G

NC_000007.14:g.140783108T>C

CM000669.2:g.140783108T>C

NC_000007.13:g.140482908T>C

CM000669.1:g.140482908T>C

NC_000007.12:g.140129377T>C

NG_007873.3:g.146657A>G

NM_001354609.1:c.1227A>G

NM_004333.5:c.1227A>G

NR_148928.1:n.1532A>G

ENST00000288602.10:c.1227A>G

ENST00000496384.6:n.50A>G

ENST00000497784.1:n.1262A>G

Benign

Met criteria codes **4**

BP4

BP5

BP7

BA1

Evidence Links **0**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

RASopathy VCEP

The filtering allele frequency of the c.1227A>G (p.Ser409=) variant in the BRAF gene is 0.313% for European (Non-Finnish) chromosomes by the Exome Aggregation Consortium (233/66620 with 95% CI), which is a high enough frequency to be classified as benign based on thresholds defined by the ClinGen RASopathy Expert panel for autosomal dominant RASopathy variants (BA1). Additionally, this variant is a synonymous (silent) variant at a nucleotide that is not highly conserved and is not predicted to impact splicing (BP7). The p.Ser409= variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM, EGL Genetics internal data; GTR ID's: 21766, 26957, 500060; SCV000057203.8; SCV000061570.5; SCV000112807.7). Computational prediction tools and conservation analysis suggest that the p.Ser409= variant does not impact the protein (BP4). In summary, this variant meets criteria to be classified as benign. ACMG/AMP criteria applied: BA1, BP7, BP5, BP4.

Met criteria codes

BP4			Computational prediction tools and conservation analysis suggest that the p.Ser409= variant does not impact the protein (BP4).
BP5			The p.Ser409= variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM, EGL Genetics internal data; GTR ID's: 21766, 26957, 500060; SCV000057203.8; SCV000061570.5; SCV000112807.7).
BP7			Additionally, this variant is a synonymous (silent) variant at a nucleotide that is not highly conserved and is not predicted to impact splicing (BP7).
BA1			The allele frequency of the c.1227A>G (p.Ser409=) variant in the BRAF gene is 1.53% (101/6602) of European (Finnish) chromosomes by the Exome Aggregation Consortium (http://exac.broadinstitute.org), which is a high enough frequency to be classified as benign based on thresholds defined by the ClinGen RASopathy Expert Panel for autosomal dominant RASopathy variants (BA1).

Curation History



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