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Variant: NM_004333.4(BRAF):c.1595G>A (p.Cys532Tyr)

CA175337

40380 (ClinVar)

Gene: BRAF (HGNC:673)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: d9ad9287-b52a-479a-8ff9-9ba17dc649ae
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HGVS expressions

NM_004333.4:c.1595G>A
NM_004333.4(BRAF):c.1595G>A (p.Cys532Tyr)
NC_000007.14:g.140777011C>T
CM000669.2:g.140777011C>T
NC_000007.13:g.140476811C>T
CM000669.1:g.140476811C>T
NC_000007.12:g.140123280C>T
NG_007873.3:g.152754G>A
NM_001354609.1:c.1595G>A
NM_004333.5:c.1595G>A
NR_148928.1:n.1900G>A
NM_001354609.2:c.1595G>A
NM_001374244.1:c.1715G>A
NM_001374258.1:c.1715G>A
NM_004333.6:c.1595G>A
ENST00000288602.10:c.1595G>A
ENST00000496384.6:n.418G>A
ENST00000497784.1:n.1630G>A

Likely Pathogenic

Met criteria codes 5

PS4_Moderate PP3 PP2 PM6 PM2

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.1595G>A (p.Cys532Tyr) variant in BRAF has been observed in three probands with RASopathies (PS4_Moderate; Laboratory for Molecular Medicine, Hopital Universitaire Robert Debre internal data, ClinVar SCV000197143.4) It has also been seen as an unconfirmed de novo occurrence in a patient with clinical features of a RASopathy (PM6; EGL internal data, ClinVar SCV000112809.8). This variant was absent from large population studies (PM2; gnomad.broadinstitute.org). 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). Computational prediction tools and conservation analysis suggest that the p.Cys532Tyr variant may impact the protein (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for RASopathies in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): PS4_Moderate, PM2, PM6, PP2, PP3.

Met criteria codes

PS4_Moderate	✔	The c.1595G>A (p.Cys532Tyr) variant in BRAF has been observed in three probands with RASopathies (PS4_Moderate; Laboratory for Molecular Medicine, Hopital Universitaire Robert Debre internal data, ClinVar SCV000197143.4)
PP3	✔	Computational prediction tools and conservation analysis suggest that the p.Cys532Tyr variant may impact the protein (PP3).
PP2	✔	This variant is located in BRAF, 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).
PM6	✔	The c.1595G>A (p.Cys532Tyr) variant in BRAF has been reported as an unconfirmed de novo occurrence in a patient with clinical features of a RASopathy (PM6; EGL internal data, ClinVar SCV000112809.8).
PM2	✔	Absent from both versions of gnomAD.

Curation History

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