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Variant: NM_004333.4(BRAF):c.730A>C (p.Thr244Pro)

CA280025

40346 (ClinVar)

Gene: BRAF (HGNC:673)
Condition: cardiofaciocutaneous syndrome (MONDO:0015280)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4581b48f-d077-4114-baf4-9c4b42fd49c4
Approved on: 2017-04-03
Published on: 2018-12-10

HGVS expressions

NM_004333.4:c.730A>C
NM_004333.4(BRAF):c.730A>C (p.Thr244Pro)
NC_000007.14:g.140801542T>G
CM000669.2:g.140801542T>G
NC_000007.13:g.140501342T>G
CM000669.1:g.140501342T>G
NC_000007.12:g.140147811T>G
NG_007873.3:g.128223A>C
NM_001354609.1:c.730A>C
NM_004333.5:c.730A>C
NR_148928.1:n.1035A>C
ENST00000288602.10:c.730A>C
ENST00000497784.1:n.765A>C

Pathogenic

Met criteria codes 6

PS2 PP3 PP2 PM2 PM6 PM1

Not Met criteria codes 1

PS3

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.730A>C (p.Thr244Pro) variant in BRAF has been reported in the literature as a de novo occurrence in at least 2 patients with clinical features of a RASopathy (PM6 and PS2; PMID 17551924 and 18042262). This variant was absent from large population studies (PM2; ExAC, http://exac.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). This variant is in a location which has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of BRAF (PM1; PMID 29493581). Computational prediction tools and conservation analysis suggest that the p.Thr244Pro variant may impact the protein (PP3).

In summary, this variant meets criteria to be classified as pathogenic for RASopathies in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): PP2, PP3, PM1, PM2, PM6, PS2.

Met criteria codes

PS2	✔	The p.T244P variant in BRAF has been reported in the literature as a de novo occurrence in at least 2 patients with clinical features of a RASopathy (PM6 and PS2; PMID 17551924 and 18042262)
PP3	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	✔	The p.T244P variant in BRAF has been reported in the literature as a de novo occurrence in at least 2 patients with clinical features of a RASopathy (PM6 and PS2; PMID 17551924 and 18042262)
PM1	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Not Met criteria codes

PS3	✖	unpublished Rauen data, can't apply yet

Curation History

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