

## Variant: *NM\_004333.4(BRAF):c.770A>G (p.Gln257Arg)*

CA222583 [↗](#)

13973 (ClinVar) [↗](#)

**Gene:** BRAF (HGNC:673)

**Condition:** cardiofaciocutaneous syndrome (MONDO:0015280)

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 5f9417cc-43e4-41be-b920-ae6db397bdaa

**Approved on:** 2017-04-03

**Published on:** 2018-12-10

### HGVS expressions

**NM\_004333.4:c.770A>G**

NM\_004333.4(BRAF):c.770A>G (p.Gln257Arg)

NM\_001354609.1:c.770A>G

NM\_004333.5:c.770A>G

NR\_148928.1:n.1075A>G

ENST00000288602.10:c.770A>G

ENST00000497784.1:n.805A>G

NC\_000007.14:g.140801502T>C

CM000669.2:g.140801502T>C

NC\_000007.13:g.140501302T>C

CM000669.1:g.140501302T>C

NC\_000007.12:g.140147771T>C

NG\_007873.3:g.128263A>G

**Pathogenic**

Met criteria codes **6**

PM2 PS3 PM1 PS2\_Very Strong  
PP3 PP2

Evidence Links **5**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

### RASopathy VCEP

The c.770A>G (p.Gln257Arg) variant in BRAF has been reported in the literature as a confirmed de novo occurrence in at least 2 patients with clinical features of a RASopathy (PS2\_VeryStrong; PMID:18042262, PMID:17551924, PMID:16474404). In vitro functional studies provide some evidence that the p.Q257R variant may impact protein function (PS3; PMID:18413255; PMID:19376813). 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). Furthermore, this variant is located in exon 6, 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.Q257R variant may impact the protein (PP3). In summary, this variant meets criteria to be classified as pathogenic for cardio-facio-cutaneous syndrome in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): PP2, PP3, PM1, PM2, PS3, PS2\_VeryStrong.

### Met criteria codes

<b>PM2</b>	✓	Absent
<b>PS3</b>	✓	Phosphorylation of myelin basic protein in a coupled MEK/ERK2 kinase assay <a href="#">PubMed:19376813</a> MEK assay <a href="#">PubMed:18413255</a>
<b>PM1</b>	✓	Exon 6
<b>PS2_Very Strong</b>	✓	At least 2 de novo occurrences <hr/> De novo occurrence <a href="#">PubMed:18042262</a> De novo occurrence <a href="#">PubMed:16474404</a> De novo occurrence <a href="#">PubMed:17551924</a>
<b>PP3</b>	✓	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PP2</b>	✓	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

### Curation History [↗](#)

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.