The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

# *Variant: NM_004333.6(BRAF):c.1799T>G (p.Val600Gly)*

Version: 1.0

*CA281998*

*40389 (ClinVar)*

**Gene**: BRAF (HGNC:673)
**Condition**: RASopathy (MONDO:0021060)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 33e1b46e-d087-4f11-a5d3-ab591b3261a1
**Approved on**: 2020/6/25
**Published on**: 2020/6/25

## *HGVS expressions*

**NM_004333.6(BRAF):c.1799T>G (p.Val600Gly)**
**NM_004333.6:c.1799T>G**
NC_000007.14:g.140753336A>C
CM000669.2:g.140753336A>C
NC_000007.13:g.140453136A>C
CM000669.1:g.140453136A>C
NC_000007.12:g.140099605A>C
NG_007873.3:g.176429T>G
ENST00000646891.2:c.1799T>G
ENST00000288602.11:c.1919T>G
ENST00000479537.6:c.469T>G
ENST00000496384.7:c.1799T>G
ENST00000497784.2:c.*1249T>G
ENST00000642228.1:c.*877T>G
ENST00000642875.1:n.1259-3918T>G
ENST00000644120.1:n.2189T>G
ENST00000644650.1:c.895T>G
ENST00000644905.1:n.2681T>G
ENST00000644969.2:c.1919T>G
ENST00000646730.1:c.*375T>G
ENST00000646891.1:c.1799T>G
ENST00000647434.1:c.738-3918T>G
ENST00000288602.10:c.1799T>G
ENST00000479537.5:c.83T>G
ENST00000496384.6:c.622T>G
ENST00000497784.1:c.1834T>G
NM_004333.4:c.1799T>G
NM_001354609.1:c.1799T>G
NM_004333.5:c.1799T>G
NR_148928.1:n.2897T>G
NM_001354609.2:c.1799T>G
NM_001374244.1:c.1919T>G
NM_001374258.1:c.1919T>G
NM_001378467.1:c.1808T>G
NM_001378468.1:c.1799T>G
NM_001378469.1:c.1733T>G
NM_001378470.1:c.1697T>G

NM_001378471.1:c.1688T>G
NM_001378472.1:c.1643T>G
NM_001378473.1:c.1643T>G
NM_001378474.1:c.1799T>G
NM_001378475.1:c.1535T>G

**Pathogenic**

**Met criteria codes** 7

PM1 PM6 PM2 PS3 PP2 PP3 PS4_Supporting

Evidence Links 1

Expert Panel

RASopathy VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***RASopathy VCEP***

**The c.1799T>G (p.Val600Gly) variant in BRAF is absent from gnomAD (PM2). It has been identified in one individual with Cardiofaciocutaneous syndrome (PS4_Supporting; PMID: 20735442). It has also been reported in the literature as an unconfirmed de novo occurrence (PM6; GeneDx internal communication). In vitro functional studies provide some evidence that the p.Val600Gly variant may impact protein function (PS3; PMID: 20735442). Furthermore, the variant is in a location that 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.Val600Gly variant may impact the protein (PP3). Finally, the 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). 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): PS3, PM1, PM2, PM6, PS4_Supporting, PP3, PP2.**

**Met criteria codes**

| | | |
|---|---|---|
| **PM1** | ✔ | CR3 activation segment mutational hotspot |
| **PM6** | ✔ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM2** | ✔ | Absent from gnomAD v2.1.1 and v3 |
| **PS3** | ✔ | BRAF p.V600G mutant HEK 293T cells had increased ERK phosphorylation compared to the level induced by wild-type BRAF or the CFC kinase-impaired mutant control. In addition, the level of ERK phosphorylation induced by BRAF p.V600G was less than that of the known cancer-associated BRAF p.V600E mutant and the BRAF p.S365A control. PubMed:20735442 |
| **PP2** | ✔ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP3** | ✔ | REVEL: 0.925 |

**PS4_Supporting** ✔ PubMed:20735442

## 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.

ClinGen Terms of Use.

¤ Powered by BCM's Genboree.