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.793G>C (p.Gly265Arg)

Version: 1.0

CA261666

44832 (ClinVar)

Gene: BRAF (HGNC:673)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: 36ccb1ce-1912-4c71-8267-399b17f45c37
Approved on: 2020/7/1
Published on: 2020/7/1

HGVS expressions

NM_004333.6:c.793G>C
NM_004333.6(BRAF):c.793G>C (p.Gly265Arg)
NC_000007.14:g.140801479C>G
CM000669.2:g.140801479C>G
NC_000007.13:g.140501279C>G
CM000669.1:g.140501279C>G
NC_000007.12:g.140147748C>G
NG_007873.3:g.128286G>C
ENST00000646891.2:c.793G>C
ENST00000288602.11:c.793G>C
ENST00000496384.7:c.793G>C
ENST00000497784.2:c.*243G>C
ENST00000642228.1:c.793G>C
ENST00000642272.1:n.825G>C
ENST00000642875.1:n.287G>C
ENST00000643356.1:n.394G>C
ENST00000644120.1:n.1235G>C
ENST00000644905.1:n.882G>C
ENST00000644969.2:c.793G>C
ENST00000646730.1:c.793G>C
ENST00000646891.1:c.793G>C
ENST00000288602.10:c.793G>C
ENST00000497784.1:c.828G>C
NM_004333.4:c.793G>C
NM_001354609.1:c.793G>C
NM_004333.5:c.793G>C
NR_148928.1:n.1098G>C
NM_001354609.2:c.793G>C
NM_001374244.1:c.793G>C
NM_001374258.1:c.793G>C
NM_001378467.1:c.802G>C
NM_001378468.1:c.793G>C
NM_001378469.1:c.793G>C
NM_001378470.1:c.691G>C
NM_001378471.1:c.793G>C
NM_001378472.1:c.637G>C
NM_001378473.1:c.637G>C

NM_001378474.1:c.793G>C
NM_001378475.1:c.529G>C

Likely Pathogenic

Met criteria codes 6

PM1 PM6 PM2 PP2 PP3 PS4_Supporting

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.793G>C (p.Gly265Arg) variant in BRAF was absent from large population studies (PM2; gnomad.broadinstitute.org). It was observed as a de novo occurrence in one proband diagnosed with a RASopathy (PM6, PS4_Supporting; Laboratory for Molecular Medicine internal data, ClinVar SCV000061628.5). 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, 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.Gly265Arg variant may impact the protein (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for autosomal dominant RASopathy. RASopathy-specific ACMG/AMP criteria applied (PMID:29493581): PS4_Supporting, PM1, PM2, PM6, PP2, PP3.

Met criteria codes

PM1	✔	Occurs in exon 6 of BRAF, which has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of BRAF (PM1; PMID: 29493581).
PM6	✔	1 de novo case with Noonan syndrome.
PM2	✔	Absent from both versions of gnomAD.
PP2	✔	BRAF is a missense-constrained gene (PMID:29493581).
PP3	✔	REVEL 0.917. Entirely conserved in UCSC database. Alamut does not predict an impact to splicing.
PS4_Supporting	✔	Observed in 1 proband with Noonan syndrome.

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.