Variant: NM_002524.5(NRAS):c.36T>G (p.Gly12=)

Version: 1.1

CA1020785

380330 (ClinVar)

Gene: NRAS (HGNC:4893)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: ad2bde3b-62c8-47ab-b5aa-eb017fb556c8
Approved on: 2024-09-17
Published on: 2024-10-01

HGVS expressions

NM_002524.5:c.36T>G
NM_002524.5(NRAS):c.36T>G (p.Gly12=)
NC_000001.11:g.114716125A>C
CM000663.2:g.114716125A>C
NC_000001.10:g.115258746A>C
CM000663.1:g.115258746A>C
NC_000001.9:g.115060269A>C
NG_007572.1:g.5770T>G
ENST00000369535.5:c.36T>G
ENST00000369535.4:c.36T>G
NM_002524.4:c.36T>G

Benign

Met criteria codes 3

BP7 **BP4** **BA1**

Not Met criteria codes 2

PM2 **BS1**

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen RASopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for NRAS Version 2.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

RASopathy VCEP

The c.36T>G (p.Gly12=) variant in NRAS is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by UCSC Genome Browser (BP4, BP7). The highest population minor allele frequency in gnomAD v2.1.1 is 0.0011 (18/10370 alleles) in the Ashkenazi Jewish population, which is higher than the ClinGen RASopathy VCEP threshold (>0.0005) for BA1, and therefore meets this criterion (BA1). In summary, this variant meets the criteria to be classified as benign for autosomal dominant RASopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy VCEP: BA1, BP4, BP7. (RASopathy VCEP specifications version 2.1; 9/17/2024)

Met criteria codes

BP7	ⓘ	✓	The c.36T>G (p.Gly12=) variant in NRAS is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by UCSC Genome Browser (BP4, BP7).
BP4	ⓘ	✓	The c.36T>G (p.Gly12=) variant in NRAS is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by UCSC Genome Browser (BP4, BP7).
BA1	ⓘ	✓	The highest population minor allele frequency in gnomAD v2.1.1 is 0.0011 (18/10370 alleles) in the Ashkenazi Jewish population, which is higher than the ClinGen RASopathy VCEP threshold (>0.0005) for BA1, and therefore meets this criterion (BA1).

Not Met criteria codes

PM2		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ⓘ	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 2 of 2 rows
