

Variant: NM_002524.5(NRAS):c.360G>A (p.Leu120=)

Version: 1.1

CA134569 [↗](#)

40476 (ClinVar) [↗](#)

Gene: NRAS ([HGNC:4893](#))

Condition: RASopathy ([MONDO:0021060](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: d558c042-a22e-493d-9b5b-4a98819adf41

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HGVS expressions

NM_002524.5(NRAS):c.360G>A (p.Leu120=)

NM_002524.5:c.360G>A

NC_000001.11:g.114709659C>T

CM000663.2:g.114709659C>T

NC_000001.10:g.115252280C>T

CM000663.1:g.115252280C>T

NC_000001.9:g.115053803C>T

NG_007572.1:g.12236G>A

ENST00000369535.5:c.360G>A

ENST00000369535.4:c.360G>A

NM_002524.4:c.360G>A

Likely Benign

Met criteria codes **4**

BS1 BP5 BP7 BP4

Not Met criteria codes **3**

PM2 BA1 PP3

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 2.3.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

RASopathy VCEP

The NM_002524.5:c.360G>A (p.Leu120=) variant is a synonymous (silent) variant in NRAS 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 filtering allele frequency (the lower threshold of the 95% CI of 77/129188) of the c.360G>A variant in NRAS is 0.0004832 for European (non-Finnish) chromosomes by gnomAD v2.1.1, which is higher than the ClinGen RASopathy VCEP threshold (≥ 0.00025) for BS1, and therefore meets this criterion (BS1). Observed in 1 individual with a co-occurring likely pathogenic/pathogenic variant in a gene that explains their condition, Noonan syndrome (Invitae internal data, ClinVar SCV000253394.6). In summary, this variant meets the criteria to be classified as likely

benign for autosomal dominant RASopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy VCEP: BS1, BP4, BP5, BP7. (ClinGen RASopathy VCEP specifications version 2.3; 12/3/2024)

Met criteria codes

BS1			The filtering allele frequency (the lower threshold of the 95% CI of 77/129188) of the c.360G>A variant in NRAS is 0.0004832 for European (non-Finnish) chromosomes by gnomAD v2.1.1, which is higher than the ClinGen RASopathy VCEP threshold (≥ 0.00025) for BS1, and therefore meets this criterion (BS1).
BP5			Observed in 1 individual with a co-occurring likely pathogenic/pathogenic variant in a gene that explains their condition, Noonan syndrome (Invitae internal data, ClinVar SCV000253394.6).
BP7			The c.360G>A (p.Leu120=) variant 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.360G>A (p.Leu120=) variant 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).

Not Met criteria codes

PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			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

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