

Variant: NM_002524.5(NRAS):c.159G>A (p.Leu53=)

Version: 1.1

CA177515 [↗](#)

164807 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 6db104c5-3d96-463b-8fb7-7ff42dc61863

Approved on: 2024/12/3

Published on: 2025/3/26

HGVS expressions

NM_002524.5:c.159G>A

NM_002524.5(NRAS):c.159G>A (p.Leu53=)

NC_000001.11:g.114713931C>T

CM000663.2:g.114713931C>T

NC_000001.10:g.115256552C>T

CM000663.1:g.115256552C>T

NC_000001.9:g.115058075C>T

NG_007572.1:g.7964G>A

ENST00000369535.5:c.159G>A

ENST00000369535.4:c.159G>A

NM_002524.4:c.159G>A

Benign

Met criteria codes **1**

BA1

Not Met criteria codes **2**

PM1

BP7

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.159G>A variant is a synonymous (silent) variant (p.Leu53=) that is not predicted by SpliceAI to impact splicing, however, this nucleotide is highly conserved. The filtering allele frequency (the lower threshold of the 95% CI of 25/19928) of the c.159G>A variant in NRAS is 0.0009003 for East Asian chromosomes by gnomAD v2.1.1, 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. (ClinGen RASopathy VCEP specifications version 2.3; 12/3/2024)

Met criteria codes

BA1			Present in 0.1255% (25/19,928) of East Asian alleles in gnomAD v2 (95% CI 0.08722%). Present in 0.06300% (3/4,762) of East Asian alleles in gnomAD v3.
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Not Met criteria codes

PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			PhastCons and phyloP indicate that this nucleotide is highly conserved.

Curation History



 

 

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