

Variant: *NM_002524.5(NRAS):c.553C>T (p.Pro185Ser)*

Version: 1.1

CA183538 [↗](#)

179025 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 46bd244c-2ac0-4b2b-b668-0c0991916630

Approved on: 2024/12/3

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HGVS expressions

NM_002524.5(NRAS):c.553C>T (p.Pro185Ser)

NM_002524.5:c.553C>T

NC_000001.11:g.114708552G>A

CM000663.2:g.114708552G>A

NC_000001.10:g.115251173G>A

CM000663.1:g.115251173G>A

NC_000001.9:g.115052696G>A

NG_007572.1:g.13343C>T

ENST00000369535.5:c.553C>T

ENST00000369535.4:c.553C>T

NM_002524.4:c.553C>T

Uncertain Significance

Met criteria codes **1**

BP4

Not Met criteria codes **4**

BS1

BA1

PP3

PM2

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.553C>T variant in NRAS is a missense variant predicted to cause substitution of proline by serine at amino acid 185 (p.Pro185Ser). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006663 (14/129152 alleles) in the European (non-Finnish) population (Optional: PM2_Supporting, BS1, and BA1 are not met). The computational predictor REVEL gives a score of 0.051, which is below the threshold of 0.3, evidence that does not predict a damaging effect on NRAS function (BP4). In summary, this variant meets the criteria to be classified as uncertain significance for autosomal dominant RASopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy VCEP: BP4 (ClinGen RASopathy VCEP specifications version 2.3; 12/3/2024)

Met criteria codes

BP4			The computational predictor REVEL gives a score of 0.051, which is below the threshold of 0.3, evidence that does not predict a damaging effect on NRAS function (BP4).
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Not Met criteria codes

BS1			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
PM2			The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006663 (14/129152 alleles) in the European (non-Finnish) population (Optional: PM2_Supporting, BS1, and BA1 are not met).

Curation History



 

 

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