

[CA296087](#)

[180859 \(ClinVar\)](#)

Gene: KRAS ([HGNC:3845](#))

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

Inheritance Mode: Autosomal dominant inheritance

UID: 77516727-ce20-4572-a118-1fa6f09a2a32

Approved on: 2019-09-24

Published on: 2019-10-02

HGVS expressions

NC_000012.12:g.25209854T>A
CM000674.2:g.25209854T>A
NC_000012.11:g.25362788T>A
CM000674.1:g.25362788T>A
NC_000012.10:g.25254055T>A
NG_007524.1:g.46067A>T
NG_007524.2:g.46150A>T
ENST00000557334.6:c.169A>T
ENST00000685328.1:c.508A>T
ENST00000686877.1:c.*479A>T
ENST00000687356.1:c.*206A>T
ENST00000688228.1:n.982A>T
ENST00000688940.1:c.508A>T
ENST00000690406.1:c.311A>T
ENST00000690804.1:c.*469A>T
ENST00000692768.1:c.310A>T
ENST00000693229.1:c.433A>T
ENST00000256078.10:c.*62A>T
ENST00000311936.8:c.508A>T
ENST00000256078.8:c.*62A>T
ENST00000311936.7:c.508A>T
ENST00000557334.5:c.169A>T
NM_004985.4:c.508A>T
NM_033360.3:c.*62A>T
NM_001369786.1:c.*62A>T
NM_001369787.1:c.508A>T
NM_004985.5:c.508A>T
NM_033360.4:c.*62A>T

Uncertain Significance

Met criteria codes **2**

PP2 PM2

Not Met criteria codes **2**

PS4 PM1

Evidence Links **0**

Expert Panel

[RASopathy VCEP](#)

Criteria Specification Information

[Criteria Specifications for this VCEP](#)

RASopathy VCEP

The c.508A>T (p.Met170Leu) variant in KRAS was absent from large population studies (PM2; <https://gnomad.broadinstitute.org>). It was reported in 1 individual with a presentation that lacked a clear association with a RASopathy (PS4 not applied; SCV000310757.1) Computational prediction tools and conservation analyses do not provide strong support for or against an impact to the protein. This variant is located in the KRAS 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). In summary, the clinical significance of this variant is uncertain. ACMG/AMP Criteria applied: PM2, PP2.

Met criteria codes

PP2	✓	KRAS is a missense-constrained gene.
PM2	✓	Absent from gnomAD with high coverage.

Not Met criteria codes

PS4	✗	Observed in 1 Irish/German/Bolivian/Czech/Jewish individual, 6 years old at time of testing, presenting with ptosis and pectus excavatum (PreventionGenetics internal data; SCV000310757.1). However, this information is not specific enough to apply PS4.
PM1	✗	Does not occur at G12, G13, V14, T58, A59, G60, Q61, E62, or E63.

Curation History [↗](#)

Showing 1 to 2 of 2 rows

--

