

Variant: *NM_033360.4(KRAS):c.194G>T (p.Ser65Ile)*

Version: 1.0

CA384152083 [↗](#)

438796 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 11365dcc-39b9-4e9d-9aa1-a14271cf89f0

Approved on: 2020/5/18

Published on: 2020/5/21

HGVS expressions

NM_033360.4:c.194G>T

NM_033360.4(KRAS):c.194G>T (p.Ser65Ile)

NC_000012.12:g.25227330C>A

CM000674.2:g.25227330C>A

NC_000012.11:g.25380264C>A

CM000674.1:g.25380264C>A

NC_000012.10:g.25271531C>A

NG_007524.1:g.28591G>T

NG_007524.2:g.28674G>T

ENST00000557334.6:c.112-17419G>T

ENST00000685328.1:c.194G>T

ENST00000686877.1:c.*165G>T

ENST00000687356.1:c.112-1557G>T

ENST00000688228.1:n.668G>T

ENST00000688940.1:c.194G>T

ENST00000690804.1:c.*155G>T

ENST00000692768.1:c.-5G>T

ENST00000693229.1:c.119G>T

ENST00000256078.10:c.194G>T

ENST00000311936.8:c.194G>T

ENST00000256078.8:c.194G>T

ENST00000311936.7:c.194G>T

ENST00000557334.5:c.112-17419G>T

NM_004985.4:c.194G>T

NM_033360.3:c.194G>T

NM_001369786.1:c.194G>T

NM_001369787.1:c.194G>T

NM_004985.5:c.194G>T

Likely Pathogenic

Met criteria codes **4**

PS4_Supporting

PS2

PP2

PM2

Evidence Links **0**

Expert Panel

RASopathy VCEP [↗](#)

Criteria Specification Information **!**

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

RASopathy VCEP

The c.194G>T (p.Ser65Ile) variant in KRAS was absent from large population studies (PM2; gnomAD, <http://gnomad.broadinstitute.org>). It has been reported in 2 probands with clinical features of a RASopathy (PS4_Supporting; SCV000599968.1, PMID: 26822237, 25326635, Invitae internal data). The variant arose de novo in one of the probands with confirmed parentage (PS2; SCV000599968.1, PMID:26822237, 25326635). The variant is located in KRAS, 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, this variant meets criteria to be classified as likely pathogenic for RASopathies in an autosomal dominant manner. RASopathy-specific ACMG/AMP criteria applied (PMID:29493581):, PS2, PS4_Supporting, PM2, PP2.

Met criteria codes

PS4_Supporting			Seen once, de novo, in 9yo female with delayed motor milestones, delayed speech, developmental regression, hypotonia, hypertelorism, short stature, macrocephaly, joint contractures at elbows and hips, failure to thrive, ptosis, pulmonary stenosis, pelvic osteopenia, mild scoliosis and plexiform neurofibroma.(SCV000599968.1) Invitae: One juvenile male with congenital pulmonary valve stenosis, macrocephaly, gross motor delay
PS2			SCV000599968.1
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			Absent from gnomAD

Curation History



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