The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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

PS2 PP2 PM2 PS4_Supporting

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

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

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
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

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.