

Variant: NM_005633.3(SOS1):c.508A>G (p.Lys170Glu)

CA235342 [↗](#)

40651 (ClinVar) [↗](#)

Gene: SOS1 ([HGNC:6654](#))

Condition: Noonan syndrome ([MONDO:0018997](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 07b0e3e7-5c67-41c3-a988-3c438dfba738

Approved on: 2017-04-03

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HGVS expressions

NM_005633.3:c.508A>G

NM_005633.3(SOS1):c.508A>G (p.Lys170Glu)

NC_000002.12:g.39056704T>C

CM000664.2:g.39056704T>C

NC_000002.11:g.39283845T>C

CM000664.1:g.39283845T>C

NC_000002.10:g.39137349T>C

NG_007530.1:g.68760A>G

ENST00000395038.6:c.508A>G

ENST00000402219.6:c.508A>G

ENST00000426016.5:c.508A>G

Pathogenic

Met criteria codes **6**

PS3

PP3

PP2

PM6

PM2

PM1

Evidence Links **5**

Expert Panel

[RASopathy VCEP](#) [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

RASopathy VCEP

The c.508A>G (p.Lys170Glu) variant in **SOS1** has been reported in the literature as an unconfirmed de novo occurrence in a patient with clinical features of a RASopathy (PM6; PMID 19020799, 21387466). In vitro functional studies provide some evidence that the p.Lys170Glu variant may impact protein function (PS3; PMID 21784453, 23487764). This variant was absent from large population studies (PM2; ExAC, <http://exac.broadinstitute.org>). The variant is located in the **SOS1** 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). Furthermore, the variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of **SOS1** (PM1; PMID 29493581). Computational prediction tools and conservation analysis suggest that the p.Lys170Glu variant may impact the protein (PP3). In summary, this variant meets criteria to be classified as pathogenic for RASopathies in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): **PP2, PP3, PM1, PM2, PM6, PS3**.

Met criteria codes

PS3



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PP3



Computational prediction tools and conservation analysis suggest that the p.Lys170Glu variant may impact the protein (PP3).

PP2



The variant is in **SOS1**, which has been defined by the ClinGen RASopathy Expert Panel as a gene with low rate of benign missense with missense variants commonly being pathogenic (PP2; PMID 29493581).

PM6



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[PubMed:21387466](#)

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[PubMed:19020799](#)

PM2



This variant was absent from large population studies (PM2; ExAC, <http://exac.broadinstitute.org>).

PM1



Furthermore, the variant is in a location that has been defined by the ClinGen RASopathy Expert Panel to be a mutational hotspot or domain of **SOS1** (PM1; PMID 29493581)

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