

Variant: NM_007373.3(SHOC2):c.10A>C (p.Ser4Arg)

CA136657 [↗](#)

40635 (ClinVar) [↗](#)

Gene: SHOC2 ([HGNC:8036](#))

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

Inheritance Mode: Autosomal dominant inheritance

UUID: f8ec95a4-b09f-4a17-984e-06b4098449c2

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HGVS expressions

NM_007373.3(SHOC2):c.10A>C (p.Ser4Arg)

NM_007373.3:c.10A>C

NC_000010.11:g.110964368A>C

CM000672.2:g.110964368A>C

NC_000010.10:g.112724126A>C

CM000672.1:g.112724126A>C

NC_000010.9:g.112714116A>C

NG_028922.1:g.49826A>C

ENST00000265277.10:c.10A>C

ENST00000451838.2:c.-242-36047A>C

ENST00000480155.2:n.246A>C

ENST00000685059.1:c.10A>C

ENST00000685613.1:c.10A>C

ENST00000687592.1:n.309A>C

ENST00000688928.1:c.10A>C

ENST00000689118.1:c.10A>C

ENST00000689300.1:c.10A>C

ENST00000689997.1:c.-380-21260A>C

ENST00000691151.1:n.302A>C

ENST00000691369.1:c.10A>C

ENST00000691441.1:c.10A>C

ENST00000691903.1:c.10A>C

ENST00000692776.1:c.10A>C

ENST00000369452.9:c.10A>C

ENST00000265277.9:c.10A>C

ENST00000369452.8:c.10A>C

ENST00000480155.1:n.494A>C

ENST00000489390.1:n.56-36047A>C

ENST00000489783.1:n.388A>C

NM_001269039.1:c.10A>C

NM_001269039.2:c.10A>C

NM_001324336.1:c.10A>C

NM_001324337.1:c.10A>C

NR_136749.1:n.116-21260A>C

NM_007373.4:c.10A>C

NM_001269039.3:c.10A>C

NM_001324336.2:c.10A>C

NM_001324337.2:c.10A>C
NR_136749.2:n.55-21260A>C

Benign

Met criteria codes **3**

BP5 BP4 BA1

Not Met criteria codes **4**

PM2 BS1 BP2 PP3

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 SHOC2 Version 2.1.0*

[↗](#) **Criteria Specification Approval History**

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

Evidence submitted by expert panel

RASopathy VCEP

The c.10A>C variant in the SHOC2 gene is a missense variant predicted to cause substitution of serine by arginine at amino acid 4 (p.Ser4Arg). The highest filtering allele frequency in gnomAD v4.1.0 is 0.2286% (124/59742 alleles) in the Admixed American population and therefore meets this criterion (BA1). The computational predictor tool REVEL gives a score of 0.113 and does not predict a damaging effect on SHOC2 function (BP4). This variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM GTR Lab ID: 26957, 21766 internal data; ClinVar SCV000209046.7, SCV000062455.5). In summary, this variant meets criteria to be classified as benign for autosomal dominant RASopathies based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy Variant Curation Expert Panel: BA1, BP4, BP5 (Specification Version 2.1, 09/17/2024)

Met criteria codes

BP5		✓	The variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM GTR Lab ID: 26957, 21766 internal data; ClinVar SCV000209046.7, SCV000062455.5).
BP4		✓	The computational predictor tool REVEL gives a score of 0.113 and does not predict a damaging effect on function (BP4)
BA1		✓	The highest filtering allele frequency in gnomAD v4.1.0 is 0.2286% (124/59742 alleles) in the Admixed American population and therefore meets this criterion (BA1).

Not Met criteria codes

PM2		✗	The highest filtering allele frequency in gnomAD v4.1.0 is 0.2286% (124/59742 alleles) in the Admixed American population (BA1).
BS1		✗	The highest filtering allele frequency in gnomAD v4.1.0 is 0.2286% (124/59742 alleles) in the Admixed American population (BA1).

BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			The computational predictor tool REVEL gives a score of 0.113 and does not predict a damaging effect on function (BP4)

Curation History 		
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