

Variant: NM_007373.3(SHOC2):c.4A>G (p.Ser2Gly)

CA118524 [↗](#)

6821 (ClinVar) [↗](#)

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

Condition: Noonan syndrome-like disorder with loose anagen hair 1 ([MONDO:0054637](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 39b0e509-abdb-415d-87bd-98b7310bb1c0

Approved on: 2017-04-03

Published on: 2018-12-10

HGVS expressions

NM_007373.3(SHOC2):c.4A>G (p.Ser2Gly)

NM_007373.3:c.4A>G

NC_000010.11:g.110964362A>G

CM000672.2:g.110964362A>G

NC_000010.10:g.112724120A>G

CM000672.1:g.112724120A>G

NC_000010.9:g.112714110A>G

NG_028922.1:g.49820A>G

NM_001269039.1:c.4A>G

NM_001269039.2:c.4A>G

NM_001324336.1:c.4A>G

NM_001324337.1:c.4A>G

NR_136749.1:n.116-21266A>G

ENST00000265277.9:c.4A>G

ENST00000369452.8:c.4A>G

ENST00000480155.1:n.488A>G

ENST00000489390.1:n.56-36053A>G

ENST00000489783.1:n.382A>G

Pathogenic

Met criteria codes **5**

PS2_Very Strong

PS3

PS4

PP2

PM2

Evidence Links **6**

Expert Panel

[RASopathy VCEP](#) [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

RASopathy VCEP

The c.4A>G (p.Ser2Gly) variant in SHOC2 has been reported as a confirmed de novo occurrence in multiple patients with clinical features of a RASopathy (PS2_VeryStrong; Partners LMM, Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal data; GTR ID's: 21766, 506381, 28338; ClinVar SCV000062456.5, SCV000209051.10, SCV000263045.1 PMID 19684605, 21548061, 23918763, 22528146). The p.Ser2Gly variant has been identified in at least 5 independent occurrences in patients with clinical features of a RASopathy (PS4; Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal

data GTR ID's: 506381, 28338; PMID: 25563136, 24458587). In vitro functional studies provide some evidence that the p.Ser2Gly variant may impact protein function (PS3; PMID: 19684605). This variant was absent from large population studies (PM2; ExAC, <http://exac.broadinstitute.org>). The variant is located in the SHOC2 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, this variant meets criteria to be classified as pathogenic for RASopathies in an autosomal dominant manner. Rasopathy-specific ACMG/AMP criteria applied (PMID:29493581): PS2_VeryStrong, PS3, PS4, PM2, PP2.

Met criteria codes

PS2_Very Strong			The c.4A>G (p.Ser2Gly) variant in SHOC2 has been reported as a confirmed de novo occurrence in a patient with clinical features of a RASopathy (PS2_VeryStrong; Partners LMM, Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal data; GTR ID's: 21766, 506381, 28338; ClinVar SCV000062456.5, SCV000209051.10, SCV000263045.1 PMID 19684605, 21548061, 23918763, 22528146).
			de novo case PubMed:22528146 
			de novo case PubMed:23918763 
			de novo case PubMed:19684605 
			de novo case PubMed:21548061 
PS3			In vitro functional studies provide some evidence that the p.Ser2Gly variant may impact protein function (PS3; PMID: 19684605).
			In vitro functional studies provide some evidence that the p.Ser2Gly variant may impact protein function (PS3; PMID: 19684605). PubMed:19684605 
PS4			The p.Ser2Gly variant has been identified in at least 5 independent occurrences in patients with clinical features of a RASopathy (PS4; Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal data GTR ID's: 506381, 28338; PMID: 25563136, 24458587)
			The p.Ser2Gly variant has been identified in at least 5 independent occurrences in patients with clinical features of a RASopathy (PS4; Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal data GTR ID's: 506381, 28338; PMID: 25563136, 24458587) PubMed:25563136 
			The p.Ser2Gly variant has been identified in at least 5 independent occurrences in patients with clinical features of a RASopathy (PS4; Institute of Human Genetics, Otto von Guericke University Magdeburg, APHP-Robert Debré Hospital internal data GTR ID's: 506381, 28338; PMID: 25563136, 24458587) PubMed:24458587 
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

▼

▼

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.