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# *Variant: NM_006939.4(SOS2):c.800T>A (p.Met267Lys)*

Version: 1.0

*CA204984*

*209092 (ClinVar)*

**Gene**: SOS2 (HGNC:6655)
**Condition**: RASopathy (MONDO:0021060)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 50413a95-4bb5-4541-8121-2efb05178517
**Approved on**: 2024/9/17
**Published on**: 2024/10/1

## *HGVS expressions*

**NM_006939.4(SOS2):c.800T>A (p.Met267Lys)**
**NM_006939.4:c.800T>A**
NC_000014.9:g.50182521A>T
CM000676.2:g.50182521A>T
NC_000014.8:g.50649239A>T
CM000676.1:g.50649239A>T
NC_000014.7:g.49718989A>T
NG_051073.1:g.54173T>A
ENST00000216373.10:c.800T>A
ENST00000216373.9:c.800T>A
ENST00000543680.5:c.800T>A
ENST00000556469.5:n.567T>A
NM_006939.2:c.800T>A
NM_006939.3:c.800T>A

**Likely Pathogenic**

**Met criteria codes** 4

PS4_Moderate PS2 PM2_Supporting 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 SOS2 Version 2.1.0*
**Criteria Specification Approval History**
**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***RASopathy VCEP***

**The c.800T>A variant in SOS2 (NM_006939.4(SOS2):c.800T>A (p.Met267Lys)) is a missense variant predicted to cause substitution of methionine by lysine at amino acid 267. It has been identified in at least 3 probands with clinical features of a RASopathy (PS4_Moderate; SCV001426180.1, PMIDs: 25795793, 30707178). Two of these cases were reported as de novo occurrences, one with maternity and paternity confirmation and the other without (PS2, PM6; SCV001426180.1, PMID: 25795793). The computational predictor REVEL gives a**

**score of 0.802, which is above the threshold of 0.7, evidence that correlates with impact to SOS2 function (PP3). 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: PS2, PS4_Moderate, PM2_Supporting, PP3 (Version 2.1; 9/7/2024)**

**Met criteria codes**

| | | |
|---|---|---|
| **PS4_Moderate** | ✔ | This variant has been reported in 3 probands with Noonan Syndrome (PS4_moderate; PMIDs: 25795793, 30707178 & Otto von Guericke University Magdeburg Internal Data; 3 PS4 points). |
| **PS2** | ✔ | This variant has been identified as a de novo occurrence with confirmed parental relationships in 1 individual and as a de novo occurrence with unconfirmed parental relationships in 1 individual, both with Noonan Syndrome (PS2; Otto von Guericke University Magdeburg Internal Data & PMID:25795793; 3 PS2 points). |
| **PM2_Supporting** | ✔ | Absent from gnomAD v2 and v3 |
| **PP3** | ✔ | The computational predictor REVEL gives a score of 0.802, which is above the threshold of 0.7, evidence that correlates with impact to SOS2 function (PP3). |

Curation History

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| See Report | Preferred Variant Title | Classification | Condition | Published Date | Version | Criteria Specification | Gene |
|---|---|---|---|---|---|---|---|
| View | NM_006939.4(SOS2):c.800T>A (p.Met2… | Likely Pathogenic | RASopathy | 2024-10-01 | 1.0 | ClinGen RASopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SOS2 Version 2.1.0 | SOS2 |

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