Variant: NM_006767.4(LZTR1):c.848G>A (p.Arg283Gln)

Version: 1.1

CA410781238

561716 (ClinVar)

Gene: LZTR1 (HGNC:8216)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: c8222db2-1fa0-4817-b2bb-713739454635
Approved on: 2024-12-03
Published on: 2025-03-26

HGVS expressions

NM_006767.4:c.848G>A
NM_006767.4(LZTR1):c.848G>A (p.Arg283Gln)
NC_000022.11:g.20991684G>A
CM000684.2:g.20991684G>A
NC_000022.10:g.21345973G>A
CM000684.1:g.21345973G>A
NC_000022.9:g.19675973G>A
NG_034193.1:g.14416G>A
ENST00000700578.1:c.848G>A
ENST00000495142.6:n.193G>A
ENST00000642151.1:c.679G>A
ENST00000643578.1:n.870G>A
ENST00000646124.2:c.848G>A
ENST00000646506.1:n.427G>A
ENST00000215739.12:c.848G>A
ENST00000414985.5:c.*414G>A
ENST00000479606.5:n.994G>A
ENST00000497716.5:n.675G>A
NM_006767.3:c.848G>A

Likely Pathogenic

Met criteria codes 3

PS2 PS4_Moderate PM2_Supporting

Not Met criteria codes 4

BA1 BS1 BP4 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 LZTR1 Version 1.3.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

RASopathy VCEP

The NM_006767.4:c.848G>A variant in LZTR1 is a missense variant predicted to cause substitution of arginine by glutamine at amino acid 283 (p.Arg283Gln). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.609, which is neither above nor below the thresholds predicting a damaging or benign impact on LZTR1 function. This variant has been reported in 5 probands with RASopathy (PS4_Moderate; PMID: 30368668, SCV000808536.4, GeneDx). This variant has been identified as a de novo occurrence with confirmed parental relationships in 2 individuals with RASopathy (PS2; PMID: 30368668, SCV000808536.4, GeneDx). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant RASopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy VCEP: PS2, PS4_Moderate, PM2_Supporting. (ClinGen RASopathy VCEP specifications version 1.3; 12/3/2024)

Met criteria codes

PS2	✔	This variant has been identified as a de novo occurrence with confirmed parental relationships in 2 individuals with RASopathy (PS2; PMID: 30368668, SCV000808536.4, GeneDx).
PS4_Moderate	✔	This variant has been reported in 5 probands with RASopathy (PS4_Moderate; PMID: 30368668, SCV000808536.4, GeneDx).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	The computational predictor REVEL gives a score of 0.609, which is neither above nor below the thresholds predicting a damaging or benign impact on LZTR1 function.

Curation History

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