Variant: NM_000018.4(ACADVL):c.1146G>C (p.Lys382Asn)

Version: 1.0

CA16607872

389672 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: 135b5d0f-4953-4f8d-81f6-b09d86a07858
Approved on: 2024-09-24
Published on: 2024-09-24

HGVS expressions

NM_000018.4:c.1146G>C
NM_000018.4(ACADVL):c.1146G>C (p.Lys382Asn)
NC_000017.11:g.7223201G>C
CM000679.2:g.7223201G>C
NC_000017.10:g.7126520G>C
CM000679.1:g.7126520G>C
NC_000017.9:g.7067244G>C
NG_007975.1:g.8368G>C
NG_008391.2:g.1850C>G
ENST00000356839.10:c.1146G>C
ENST00000322910.9:c.*1101G>C
ENST00000350303.9:c.1080G>C
ENST00000356839.9:c.1146G>C
ENST00000542255.6:c.4G>C
ENST00000543245.6:c.1215G>C
ENST00000578579.2:n.95G>C
ENST00000578824.5:n.562G>C
ENST00000579425.5:n.170G>C
ENST00000582379.1:n.797G>C
ENST00000583858.5:c.175G>C
ENST00000585203.6:n.354G>C
NM_000018.3:c.1146G>C
NM_001033859.2:c.1080G>C
NM_001270447.1:c.1215G>C
NM_001270448.1:c.918G>C
NM_001033859.3:c.1080G>C
NM_001270447.2:c.1215G>C
NM_001270448.2:c.918G>C

Likely Pathogenic

Met criteria codes 6

PP3 PP4 PM2_Supporting PM1 PM3 PM5_Supporting

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.1146G>C (NM_000018.4) variant in ACADVL is a missense variant predicted to cause substitution of lysine by asparagine at amino acid 382 (p.Lys382Asn). Information provided to the ACADVL VCEP provided by an external clinical laboratory shows an elevated plasma C14:1 in an individual that that had c.848T>C (p.Val283Ala) confirmed in trans (PP4, PM3). Another missense variant c.1144A>C (p.Lys382Gln) (Variation ID: 1628) in the same codon has been classified as likely pathogenic for very long chain acyl CoA dehydrogenase (VLCAD) deficiency by the ClinGen ACADVL Variant Curation Expert Panel (PM5_Supporting). This variant resides within a region, p.382, of ACADVL that is defined as a critical functional domain for FAD binding and salt-bridge interactions by the ClinGen ACADVL VCEP (PM1; PMID: 20060901). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.91, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3). In summary, this variant meets the criteria to be classified as [CLASSIFICATION] for autosomal recessive very long chain acyl-CoA dehydrogenase (VLCAD) deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen ACADVL Variant Curation Expert Panel: PM1, PM3, PM5_Supporting, PP3 PP4 (ACADVL VCEP specifications version 1; approved November 9, 2021).

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.91, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PP4	✔	Information provided to the ACADVL VCEP provided by an external clinical laboratory shows an elevated plasma C14:1 in an individual that that had c.848T>C (p.Val283Ala) confirmed in trans (PP4, PM3)
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PM1	✔	This variant resides within a region, p.382, of ACADVL that is defined as a critical functional domain for FAD binding and salt-bridge interactions by the ClinGen ACADVL VCEP (PM1; PMID: 20060901).
PM3	✔	Information provided to the ACADVL VCEP provided by an external clinical laboratory shows an elevated plasma C14:1 in an individual that that had c.848T>C (p.Val283Ala) confirmed in trans (PP4, PM3).
PM5_Supporting	✔	Another missense variant c.1144A>C (p.Lys382Gln) (Variation ID: 1628) in the same codon has been classified as likely pathogenic for very long chain acyl CoA dehydrogenase (VLCAD) deficiency by the ClinGen ACADVL Variant Curation Expert Panel (PM5_Supporting).

Curation History

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