The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000018.4(ACADVL):c.1220G>C (p.Gly407Ala)

Version: 1.0

CA287439291

474878 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: 46830bcc-6b37-4ddd-8c85-9c43a0a4c089
Approved on: 2023/2/13
Published on: 2023/2/13

HGVS expressions

NM_000018.4:c.1220G>C
NM_000018.4(ACADVL):c.1220G>C (p.Gly407Ala)
NC_000017.11:g.7223681G>C
CM000679.2:g.7223681G>C
NC_000017.10:g.7127000G>C
CM000679.1:g.7127000G>C
NC_000017.9:g.7067724G>C
NG_007975.1:g.8848G>C
NG_008391.2:g.1370C>G
NG_033038.1:g.15864C>G
ENST00000356839.10:c.1220G>C
ENST00000322910.9:c.*1175G>C
ENST00000350303.9:c.1154G>C
ENST00000356839.9:c.1220G>C
ENST00000542255.6:c.78G>C
ENST00000543245.6:c.1289G>C
ENST00000578579.2:n.391G>C
ENST00000578711.1:n.177G>C
ENST00000578824.5:n.636G>C
ENST00000579425.5:n.244G>C
ENST00000579546.1:c.57G>C
ENST00000583858.5:c.249G>C
ENST00000585203.6:n.428G>C
NM_000018.3:c.1220G>C
NM_001033859.2:c.1154G>C
NM_001270447.1:c.1289G>C
NM_001270448.1:c.992G>C
NM_001033859.3:c.1154G>C
NM_001270447.2:c.1289G>C
NM_001270448.2:c.992G>C

Likely Pathogenic

Met criteria codes 5

PM3 PP4_Moderate PP1 PP3 PM2_Supporting

Expert Panel

ACADVL VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.1220G>C (NM_000018.4) variant in ACADVL is a missense variant predicted to cause substitution of glycine by alanine at amino acid 407 (p.Gly407Ala) and is also known as Gly367Ala in the fully processed protein. This variant has been reported as occurring in trans to a known pathogenic variant in a pair of siblings with positive newborn screens and reduced very long chain acyl-CoA dehydrogenase (VLCAD) activity (PMID: 28755359, PM3, PP1, PP4_moderate). At least one individual with this variant was identified by newborn screen, but this information is insufficient to use toward classification (PMID: 26385305, 23798014). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006 in the Latino population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.803, 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 likely pathogenic for autosomal recessive VLCAD deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen ACADVL Variant Curation Expert Panel: PM2_Supporting, PM3, PP1, PP3, PP4_moderate (ACADVL VCEP specifications version 1; approved November 8, 2021).

Met criteria codes

PM3	✓	This variant has been reported as occurring in trans to a known pathogenic variant in a pair of siblings with positive newborn screens and reduced VLCAD activity (PMID: 28755359, PM3, PP4_moderate).
PP4_Moderate	✓	This variant has been reported as occurring in trans to a known pathogenic variant in a pair of siblings with positive newborn screens and reduced VLCAD activity (PMID: 28755359, PM3, PP4_moderate).
PP1	✓	The variant has been reported to segregate with very long chain acyl CoA dehydrogenase (VLCAD) deficiency in 2 affected siblings from 1 family (PP1; PMID: 28755359).
PP3	✓	The computational predictor REVEL gives a score of 0.803, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PM2_Supporting	✓	The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006 in the Latino population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting).

Curation History

Showing 1 to 1 of 1 rows

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