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Variant: NM_000018.4(ACADVL):c.619T>C (p.Ser207Pro)

Version: 1.0

CA8337769

551588 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: a8d50bf8-d177-4bc2-b8b3-245d4c748998
Approved on: 2024/2/27
Published on: 2024/2/27

HGVS expressions

NM_000018.4(ACADVL):c.619T>C (p.Ser207Pro)
NM_000018.4:c.619T>C
NC_000017.11:g.7221679T>C
CM000679.2:g.7221679T>C
NC_000017.10:g.7124998T>C
CM000679.1:g.7124998T>C
NC_000017.9:g.7065722T>C
NG_007975.1:g.6846T>C
NG_008391.2:g.3372A>G
ENST00000356839.10:c.619T>C
ENST00000322910.9:c.*574T>C
ENST00000350303.9:c.553T>C
ENST00000356839.9:c.619T>C
ENST00000543245.6:c.688T>C
ENST00000577191.5:n.696T>C
ENST00000577857.5:n.435T>C
ENST00000579286.5:n.800T>C
ENST00000579886.2:c.457T>C
ENST00000580365.1:n.350T>C
ENST00000581378.5:c.337T>C
ENST00000581562.5:n.525-273T>C
ENST00000583312.5:c.619T>C
ENST00000583760.1:n.401T>C
NM_000018.3:c.619T>C
NM_001033859.2:c.553T>C
NM_001270447.1:c.688T>C
NM_001270448.1:c.391T>C
NM_001033859.3:c.553T>C
NM_001270447.2:c.688T>C
NM_001270448.2:c.391T>C

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PP4_Moderate PM3_Strong

Expert Panel

ACADVL VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The NM_000018.4(ACADVL): c.619T>C (p.Ser207Pro) variant is a missense variant predicted to cause substitution of serine by proline at amino acid 207. At least two individuals with this variant displayed a newborn screen consistent with very long chain acyl-CoA dehydrogenase (VLCAD) deficiency as well as follow-up acylcarnitine testing showing increased C14:1 acylcarnitines, which is highly specific for VLCAD deficiency (PP4_Moderate, PMID: 26927351). This individual was compound heterozygous for this variant and a distinct pathogenic or likely pathogenic variant confirmed in trans by parental testing (PM3_Strong). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.79, 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_Strong, PP3, PP4_Moderate (ACADVL VCEP specifications version 1; approved November 9, 2021).

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.79, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PM2	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PP4_Moderate	✔	At least one patient with this variant displayed newborn screen consistent with very long chain acyl-CoA dehydrogenase (VLCAD) deficiency as well as follow-up acylcarnitine testing showing increased C14:1 acylcarnitines, which is highly specific for VLCAD deficiency (PP4_Moderate, PMID: 26927351).
PM3_Strong	✔	Confirmed in trans by parental testing to c.1770_1773del (curated by VCEP as pathogenic; cdot nomenclature confirmed by Sanger sequencing in figure 1)

Curation History

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