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.896A>T (p.Lys299Met)

Version: 1.0

CA8337902

932829 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: 37e89f02-7ef4-4e15-a98b-55c415cf8d9f
Approved on: 2023/6/13
Published on: 2023/6/13

HGVS expressions

NM_000018.4:c.896A>T
NM_000018.4(ACADVL):c.896A>T (p.Lys299Met)
NC_000017.11:g.7222684A>T
CM000679.2:g.7222684A>T
NC_000017.10:g.7126003A>T
CM000679.1:g.7126003A>T
NC_000017.9:g.7066727A>T
NG_007975.1:g.7851A>T
NG_008391.2:g.2367T>A
ENST00000356839.10:c.896A>T
ENST00000322910.9:c.*851A>T
ENST00000350303.9:c.830A>T
ENST00000356839.9:c.896A>T
ENST00000543245.6:c.965A>T
ENST00000578824.5:n.45A>T
ENST00000581378.5:c.614A>T
ENST00000582379.1:n.280A>T
NM_000018.3:c.896A>T
NM_001033859.2:c.830A>T
NM_001270447.1:c.965A>T
NM_001270448.1:c.668A>T
NM_001033859.3:c.830A>T
NM_001270447.2:c.965A>T
NM_001270448.2:c.668A>T

Likely Pathogenic

Met criteria codes 4

PM3 PP4_Moderate PP3 PM2_Supporting

Not Met criteria codes 1

PM5

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specification: *ClinGen ACADVL Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1*
PDF
Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.896A>T (p.Lys299Met) variant in ACADVL has been reported in the literature in patients with VLCAD deficiency and elevated acylcarnitine (PP4_moderate; PMID: 16982043, 35281659). The variant has also been detected in compound heterozygote with pathogenic variant p.Val283Ala (PM3; PMID: 35281659). Three missense variants (p.Lys299Asn, p.Lys299Arg, p.Lys299Glu; PMIDs: 9973285, 31737040, 33150772) in the same codon have also been reported for VLCAD deficiency. This variant is absent from gnomAD population database v2.1.1(PM2_Supporting) and the computational predictor REVEL gives a score of 0.963, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3). The ACADVL Variant Curation Expert Panel VCEP classified the variant as likely pathogenic based on (PP4_moderate, PM3, PM2_Supporting, PP3).

Met criteria codes

PM3	ℹ	✔	Found with L502Q - unknown phase. not classified by Clingen Found with p.V283A in two patients & p.R632C (not classified by Clingen) Points = 1
PP4_Moderate	ℹ	✔	Elevated C14:0, Enzyme activity 16% of control (used patient derived material) C14:1 > 1.0uM and assertion of VLCADD (patient material)
PP3	ℹ	✔	0.963 (>0.75)
PM2_Supporting	ℹ	✔	absent

Not Met criteria codes

PM5	ℹ	✖	Other missense of this codon (K299N/R/E). None classified by Clingen.

Curation History

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