

Variant: NM_000018.4(ACADVL):c.266del (p.Pro89fs)

Version: 1.0

CA8337611 [↗](#)

552361 (ClinVar) [↗](#)

Gene: ACADVL ([HGNC:37](#))

Condition: very long chain acyl-CoA dehydrogenase deficiency
([MONDO:0008723](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 66cc33f4-9274-41ae-89f4-b07a919f4d29

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HGVS expressions

NM_000018.4(ACADVL):c.266del (p.Pro89fs)

NM_000018.4:c.266del

NC_000017.11:g.7220665del

CM000679.2:g.7220665del

NC_000017.10:g.7123984del

CM000679.1:g.7123984del

NC_000017.9:g.7064708del

NG_007975.1:g.5832del

NG_008391.2:g.4388del

ENST00000356839.10:c.266del

ENST00000322910.9:c.*221del

ENST00000350303.9:c.200del

ENST00000356839.9:c.266del

ENST00000543245.6:c.335del

ENST00000577191.5:n.343del

ENST00000577433.5:n.474del

ENST00000577857.5:n.229-101del

ENST00000578269.5:n.713del

ENST00000578421.1:n.474del

ENST00000579286.5:n.447del

ENST00000579886.2:c.201+139del

ENST00000580263.5:n.430del

ENST00000581562.5:n.313del

ENST00000582056.5:n.356del

ENST00000582166.1:n.154del

ENST00000582356.5:n.465del

ENST00000583312.5:c.266del

ENST00000584103.5:c.266del

NM_000018.3:c.266del

NM_001033859.2:c.200del

NM_001270447.1:c.335del

NM_001270448.1:c.38del

NM_001033859.3:c.200del

NM_001270447.2:c.335del

NM_001270448.2:c.38del

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PM3 PP4

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.266del variant in ACADVL is a frameshift predicted to cause a premature stop codon in biologically relevant exon 4/20 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1: PMIDs 9973285, 11590124). The variant has been identified in at least one individual identified by abnormal newborn screening results suggestive of very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency without an additional ACADVL variant identified or follow-up plasma acylcarnitines (PMID: 26385305). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00005437 in East Asian population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting). To our knowledge, functional assays have not been reported for this variant. In summary, this variant meets the criteria to be classified as **LIKELY PATHOGENIC** 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: PVS1, PM2_Supporting (ACADVL VCEP specifications v2.0; Approved on 12/14/2021).

Met criteria codes

PVS1



PVS1 is met. The c.266del variant in ACADVL is a frameshift predicted to cause a premature stop codon in biologically relevant exon 4/20 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1: PMIDs 9973285, 11590124).

PM2_Supporting



PM2_Supporting is met. The highest population minor allele frequency in gnomAD v2.1.1 is 0.00005437 in East Asian population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting).

Not Met criteria codes

PM3



PM3 at any strength is not met. This variant has been detected in a heterozygous state in 1 individual with very long chain acyl CoA dehydrogenase (VLCAD) deficiency.; a second pathogenic or likely pathogenic variant was not clearly reported (PMID: 26385305).

PP4



PP4 at any strength is not met. The variant has been identified in at least one individual identified by abnormal newborn screening results suggestive of very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency without an additional ACADVL variant identified or follow-up plasma acylcarnitines (PMID: 26385305).



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