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Variant: NM_000018.4(ACADVL):c.770del (p.Asp257fs)

Version: 1.0

CA981153094

935797 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: c6f69535-1a12-44ac-9112-2dbc55515d3e
Approved on: 2023/1/10
Published on: 2023/1/10

HGVS expressions

NM_000018.4:c.770del
NM_000018.4(ACADVL):c.770del (p.Asp257fs)
NC_000017.11:g.7222194del
CM000679.2:g.7222194del
NC_000017.10:g.7125513del
CM000679.1:g.7125513del
NC_000017.9:g.7066237del
NG_007975.1:g.7361del
NG_008391.2:g.2857del
ENST00000356839.10:c.770del
ENST00000322910.9:c.*725del
ENST00000350303.9:c.704del
ENST00000356839.9:c.770del
ENST00000543245.6:c.839del
ENST00000577191.5:n.942del
ENST00000581378.5:c.488del
ENST00000582379.1:n.154del
NM_000018.3:c.770del
NM_001033859.2:c.704del
NM_001270447.1:c.839del
NM_001270448.1:c.542del
NM_001033859.3:c.704del
NM_001270447.2:c.839del
NM_001270448.2:c.542del

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

PP4

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The NM_000018.4:c.770del (p.Asp257AlafsTer19) variant in ACADVL is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 9/20 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMIDs 9973285, 11590124). At least one individual with this variant was identified by newborn screen, but this information is insufficient to use toward classification (PMID: 30194637, 20547398). Additionally, this variant was identified in an individual who reportedly had increased acylcarnities and decreased very long chain acyl-CoA dehydrogenase (VLCAD) activity, but this information was insufficient to use toward classification (PMID: 12682504). This variant is absent from gnomAD v2.1.1 (PM2_supporting). 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: PVS1, PM2_Supporting (ACADVL VCEP specifications version 1; approved November 8, 2021).

Met criteria codes

PVS1	✔	The NM_000018.4:c.770del (p.Asp257AlafsTer19) variant in ACADVL is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 9/20 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMIDs 9973285, 11590124).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_supporting).

Not Met criteria codes

PP4	✖	At least one individual with this variant was identified by newborn screen, but this information is insufficient to use toward classification (PMID: 30194637, 20547398). Additionally, this variant was identified in an individual who reportedly had increased acylcarnities and decreased very long chain acyl-CoA dehydrogenase (VLCAD) activity, but this information was insufficient to use toward classification (PMID:12682504).

Curation History

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