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Variant: NM_000018.4(ACADVL):c.364A>G (p.Asn122Asp)

Version: 1.0

CA16603209

376917 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: f3e3957f-6574-4967-8c18-68fb22f8685e
Approved on: 2022/5/6
Published on: 2022/5/10

HGVS expressions

NM_000018.4(ACADVL):c.364A>G (p.Asn122Asp)
NM_000018.4:c.364A>G
NC_000017.11:g.7220945A>G
CM000679.2:g.7220945A>G
NC_000017.10:g.7124264A>G
CM000679.1:g.7124264A>G
NC_000017.9:g.7064988A>G
NG_007975.1:g.6112A>G
NG_008391.2:g.4106T>C
ENST00000356839.10:c.364A>G
ENST00000322910.9:c.*319A>G
ENST00000350303.9:c.298A>G
ENST00000356839.9:c.364A>G
ENST00000543245.6:c.433A>G
ENST00000577191.5:n.441A>G
ENST00000577433.5:n.572A>G
ENST00000577857.5:n.293+115A>G
ENST00000579286.5:n.545A>G
ENST00000579886.2:c.202A>G
ENST00000580365.1:n.95A>G
ENST00000581378.5:c.63A>G
ENST00000581562.5:n.411A>G
ENST00000582056.5:n.547A>G
ENST00000582166.1:n.345A>G
ENST00000583312.5:c.364A>G
ENST00000584103.5:c.397A>G
NM_000018.3:c.364A>G
NM_001033859.2:c.298A>G
NM_001270447.1:c.433A>G
NM_001270448.1:c.136A>G
NM_001033859.3:c.298A>G
NM_001270447.2:c.433A>G
NM_001270448.2:c.136A>G

Met criteria codes 4

Expert Panel

Likely Pathogenic

PS3 PP3 PP4 PM2_Supporting

Evidence Links 0

ACADVL VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.364A>G (p.Asn122Asp) variant in ACADVL is a missense in exon 6. This variant has been reported as a homozygote in the literature associated with very-long chain acyl-CoA dehydrogenase deficiency (PP4; PMID: 34480364). Fatty acid oxidation (FAO) flux assay performed on patient fibroblast homozygous for this variant demonstrated severe reduction of enzyme activity (PS3, PMID: 20060901). In additon, protein production was deficient for this genotype shown by western blot (PMID: 20060901). This variant is absent from population databases gnomAD v2.1.1 (PM2_supporting). The computational predictor REVEL gives a score of 0.86, 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 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: (PP4,PP3, PS3, PM2_Supporting).

Met criteria codes

PS3	✔	Severely reduces enzyme activity in a FAO flux Severely reduced protein level by western Disrupts hydrogen bonding network of nearby residues.
PP3	✔	0.856 REVEL
PP4	✔	Detected as a homozygote in patient with VLCAD deficiency.
PM2_Supporting	✔	Absent from gnomAD

Curation History

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