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Variant: NM_000018.4(ACADVL):c.602A>G (p.Tyr201Cys)

Version: 1.0

CA397723258

932789 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: d1956c84-3f68-4c7c-a275-d88ca90be85b
Approved on: 2023/11/28
Published on: 2023/11/28

HGVS expressions

NM_000018.4(ACADVL):c.602A>G (p.Tyr201Cys)
NM_000018.4:c.602A>G
NC_000017.11:g.7221662A>G
CM000679.2:g.7221662A>G
NC_000017.10:g.7124981A>G
CM000679.1:g.7124981A>G
NC_000017.9:g.7065705A>G
NG_007975.1:g.6829A>G
NG_008391.2:g.3389T>C
ENST00000356839.10:c.602A>G
ENST00000322910.9:c.*557A>G
ENST00000350303.9:c.536A>G
ENST00000356839.9:c.602A>G
ENST00000543245.6:c.671A>G
ENST00000577191.5:n.679A>G
ENST00000577857.5:n.418A>G
ENST00000579286.5:n.783A>G
ENST00000579886.2:c.440A>G
ENST00000580365.1:n.333A>G
ENST00000581378.5:c.320A>G
ENST00000581562.5:n.525-290A>G
ENST00000583312.5:c.602A>G
ENST00000583760.1:n.384A>G
NM_000018.3:c.602A>G
NM_001033859.2:c.536A>G
NM_001270447.1:c.671A>G
NM_001270448.1:c.374A>G
NM_001033859.3:c.536A>G
NM_001270447.2:c.671A>G
NM_001270448.2:c.374A>G

Likely Pathogenic

Met criteria codes 5

PM2_Supporting | PP1 | PP3 | PP4_Moderate | PM3_Supporting

Expert Panel

ACADVL VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.602A>G (NM_000018.4) variant in ACADVL is a missense variant predicted to cause substitution of tyrosine by cysteine at amino acid 201 (p.Tyr201Cys). This variant has been detected in a set of siblings that displayed increased C14:1 on newborn screen and reduced very long chain acyl CoA dehydrogenase (VLCAD) enzyme activity, which is highly specific for VLCAD deficiency (PP4_moderate, PP1; PMID: 17457695, 14517516). These siblings were compound heterozygous for this variant and a likely pathogenic variant confirmed in trans by parental testing (PM3 0.5 points, PM3_Supporting). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.954, 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_Supporting, PP1, PP3, PP4_Moderate (ACADVL VCEP specifications version 1; approved November 9, 2021

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting)
PP1	✔	2 affected siblings from one family
PP3	✔	The computational predictor REVEL gives a score of 0.954, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PP4_Moderate	✔	increased C14:1 on newborn screen and reduced very long chain acyl CoA dehydrogenase (VLCAD) enzyme activity
PM3_Supporting	✔	Detected confirmed in trans to A490P in 2 siblings.

Curation History

Showing 1 to 1 of 1 rows

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