

Variant: *NM_000018.4(ACADVL):c.790A>G (p.Lys264Glu)*

Version: 1.0

CA397723695 [↗](#)

941106 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 81022552-83d6-4505-8366-7915d471f92a

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HGVS expressions

NM_000018.4:c.790A>G

NM_000018.4(ACADVL):c.790A>G (p.Lys264Glu)

NC_000017.11:g.7222214A>G

CM000679.2:g.7222214A>G

NC_000017.10:g.7125533A>G

CM000679.1:g.7125533A>G

NC_000017.9:g.7066257A>G

NG_007975.1:g.7381A>G

NG_008391.2:g.2837T>C

ENST00000356839.10:c.790A>G

ENST00000322910.9:c.*745A>G

ENST00000350303.9:c.724A>G

ENST00000356839.9:c.790A>G

ENST00000543245.6:c.859A>G

ENST00000577191.5:n.962A>G

ENST00000581378.5:c.508A>G

ENST00000582379.1:n.174A>G

NM_000018.3:c.790A>G

NM_001033859.2:c.724A>G

NM_001270447.1:c.859A>G

NM_001270448.1:c.562A>G

NM_001033859.3:c.724A>G

NM_001270447.2:c.859A>G

NM_001270448.2:c.562A>G

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate PS3_Supporting

PM3_Supporting PP3

PM2_Supporting

Evidence Links **0**

Expert Panel

ACADVL VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

ACADVL VCEP

The c.790A>G (NM_000018.4) variant in ACADVL is a missense variant predicted to cause substitution of lysine by glutamic acid at amino acid 264 (p.Lys264Glu). At least one patient with this variant displayed very long chain acyl-CoA dehydrogenase (VLCAD) activity <20% of normal, which is highly specific for VLCAD (PP4_Moderate, PMID: 17999356). This individual also carried a distinct pathogenic variant, though the variant was not confirmed to be in trans (PMID: 17999356; PM3_Supporting). The highest population minor allele frequency in gnomAD v2.1.1 is 0.0006 in the 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). Transient transfection of this variant into fibroblasts showed reduced very long chain acyl-CoA dehydrogenase (VLCAD) activity indicating that this variant impacts protein function (PMID: 11914034; PS3_Supporting). The computational predictor REVEL gives a score of 0.871, 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: PP4_Moderate, PM3_Supporting, PM2_supporting, PS3_Supporting (ACADVL VCEP specifications version 1; approved November 8, 2021).

Met criteria codes

PP4_Moderate			At least one patient with this variant displayed very long chain acyl-CoA dehydrogenase (VLCAD) activity <20% of normal, which is highly specific for VLCAD (PP4_Moderate, PMID: 17999356).
PS3_Supporting			Transient transfection of this variant into fibroblasts showed reduced very long chain acyl-CoA dehydrogenase (VLCAD) activity indicating that this variant impacts protein function (PMID: 11914034; PS3_Supporting).
PM3_Supporting			This variant has been detected in at least one individual with very long chain acyl CoA dehydrogenase (VLCAD) deficiency and a distinct pathogenic variant, though the variant was not confirmed to be in trans (PMID: 17999356; PM3_Supporting).
PP3			The computational predictor REVEL gives a score of 0.871, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PM2_Supporting			The highest population minor allele frequency in gnomAD v2.1.1 is 0.0006 in the 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).

Curation History

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