

Variant: NM_000018.4(ACADVL):c.425T>C (p.Phe142Ser)

Version: 1.0

CA220207 [↗](#)

92283 (ClinVar) [↗](#)

Gene: ACADVL ([HGNC:37](#))
Condition: very long chain acyl-CoA dehydrogenase deficiency ([MONDO:0008723](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: 3f32f6a5-2276-4bab-b736-853284e9704f
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HGVS expressions

NM_000018.4(ACADVL):c.425T>C (p.Phe142Ser)
NM_000018.4:c.425T>C
NC_000017.11:g.7221006T>C
CM000679.2:g.7221006T>C
NC_000017.10:g.7124325T>C
CM000679.1:g.7124325T>C
NC_000017.9:g.7065049T>C
NG_007975.1:g.6173T>C
NG_008391.2:g.4045A>G
ENST00000356839.10:c.425T>C
ENST00000322910.9:c.*380T>C
ENST00000350303.9:c.359T>C
ENST00000356839.9:c.425T>C
ENST00000543245.6:c.494T>C
ENST00000577191.5:n.502T>C
ENST00000577433.5:n.633T>C
ENST00000577857.5:n.293+176T>C
ENST00000579286.5:n.606T>C
ENST00000579886.2:c.263T>C
ENST00000580365.1:n.156T>C
ENST00000581378.5:c.124T>C
ENST00000581562.5:n.472T>C
ENST00000582056.5:n.608T>C
ENST00000582166.1:n.406T>C
ENST00000583312.5:c.425T>C
ENST00000584103.5:c.458T>C
NM_000018.3:c.425T>C
NM_001033859.2:c.359T>C
NM_001270447.1:c.494T>C
NM_001270448.1:c.197T>C
NM_001033859.3:c.359T>C
NM_001270447.2:c.494T>C
NM_001270448.2:c.197T>C

Uncertain Significance

PP3

PP4

PM2_Supporting

PM3_Supporting

Not Met criteria codes 6

PVS1

PS1

PP1

PM1

PM5

PM4

Evidence Links 0

ACADVL VCEP

Criteria Specification Information !

Criteria Specifications for this VCEP

Evidence submitted by expert panel			
ACADVL VCEP			
The c.425T>C variant in ACADVL is a missense variant predicted to cause substitution of phenylalanine by serine at amino acid 142 (p.Phe142Ser). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.94, which is above the threshold 0.75, evidence that correlates with impact to ACADVL function (PP3). At least one patient with this variant displayed organic acidemia and fatty acid oxidation issues, which are highly specific for VLCAD deficiency (PP4, PMID: 27629047, PMID: 28980192). This individual was also reported homozygous for the variant (PMID: 27629047; points=0.5; PM3_supporting). In summary, this variant meets the criteria to be classified as VUS 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: PM2,PM3_supporting PP3, PP4			
Met criteria codes			
PP3		✓	REVEL score is 0.944 which passes the ACADVL criteria of greater than 0.75
PP4		✓	One proband case was found (Saudi Arabia) and diagnosed with VLCAD deficiency. Only a phenotypic description was given - no enzyme level or acylcarnitine analysis data.
PM2_Supporting		✓	c.425T>C is not found in gnomAD or 1000 Genome projects
PM3_Supporting		✓	Described as homozygote in one patient (Table 3). 0.5 point = PM3_supporting
Not Met criteria codes			
PVS1		✗	variant is missense, not covered by PVS1
PS1		✗	No other codon change seen to cause F142S
PP1		✗	No segregation data found
PM1		✗	Phe142 is not located in a designated hotspot or functional domain
PM5		✗	No other missense change seen at this residue

PM4

Phe142Ser does not alter protein length

Curation History [↗](#)

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