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Variant: NM_000033.4(ABCD1):c.-16_10del (p.Met1fs)

Version: 1.0

CA278121

11317 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: bdb7d73c-de9f-48d0-8d4c-42d9dc330c14
Approved on: 2026/4/15
Published on: 2026/4/15

HGVS expressions

NM_000033.4:c.-16_10del
NM_000033.4(ABCD1):c.-16_10del (p.Met1fs)
NC_000023.11:g.153725251_153725276del
CM000685.2:g.153725251_153725276del
NC_000023.10:g.152990706_152990731del
CM000685.1:g.152990706_152990731del
NC_000023.9:g.152643900_152643925del
NG_009022.2:g.5384_5409del
NG_023231.1:g.4473_4498del
ENST00000218104.6:c.-16_10del
ENST00000218104.5:c.-16_10del
NM_000033.3:c.-16_10del

Likely Pathogenic

Met criteria codes 4

PP1_Strong PVS1_Moderate PP4_Moderate PM2_Supporting

Not Met criteria codes 22

PM1 PM3 PM5 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP4 BP3 BP1 BP2 BP5 BP7 PS1 PS2 PS3 PS4 PP2 PP3

Evidence Links 0

Expert Panel

Peroxisomal Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Peroxisomal Disorders VCEP

The c.-16_10del (NM_000033.4) variant in ABCD1 is a variant occurring in the 5' UTR. This variant is absent from gnomAD v2.1.1 & v3.1.2 (PM2_Supporting). This variant may cause a truncated or nonfunctional protein by altering the start codon of the coding sequence. The next in-frame methionine is located at codon 67. Disruption of the initiator codon has been observed in individual(s) with adrenomyeloneuropathy (PVS1_Moderate; PMID: 11739809, 18306728). The variant has been reported to segregate with adrenoleukodystrophy in 12 affected (genotype and phenotype positive) family members (total 52 individuals). There are 7 affected

segregations (including the proband) (PP1_Strong; PMID:11739809). At least one male patient with this variant displayed adrenomyeloneuropathy, a family history with X-linked inheritance, ABCD1 gene sequencing, and VLCFA levels in fibroblasts that were significantly higher than those from normal controls (PP4_Moderate; PMID: 11739809). In summary, this variant meets the criteria to be classified as likely pathogenic for ABCD1 deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Peroxisomal Disorders Variant Curation Expert Panel: PVS1_moderate, PM2_supporting, PP1_strong, PP4_Moderate. (ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0)

Met criteria codes

PP1_Strong	✔	The variant has been reported to segregate with adrenoleukodystrophy in 12 affected (genotype and phenotype positive) family members (total 52 individuals). There are 7 affected segregations (including the proband); PMID:11739809
PVS1_Moderate	✔	The c.-16_10del (p. Met1fs) variant in ABCD1 may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein. This sequence change affects the initiator methionine of the ABCD1 mRNA. The next in-frame methionine is located at codon 67. Disruption of the initiator codon has been observed in individual(s) with adrenomyeloneuropathy (PVS1_Moderate; PMID: 11739809, 18306728).
PP4_Moderate	✔	Utilizing the ABCD1 Phenotype Specification Table created by the ClinGen Peroxisomal Disorders VCEP, at least one male patient with this variant displayed adrenomyeloneuropathy, a family history with X-linked inheritance (and at least one affected family member was a male), ABCD1 gene sequencing, and VLCFA levels in fibroblasts that were significantly higher than those from normal controls (C26/C22 ratio 0.92 versus 0.04, respectively). Exclusion of the 4 pseudogenes (on chromosomes 2, 10, 16 & 22) is assumed to be confirmed (Information on ABCD1 pseudogenes has been available since 1997, PMID: 9215666, 35053399). (PP4_Moderate); PMID: 11739809
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1, v3.1.2 and v4.1, with good coverage (PM2_Supporting).

Not Met criteria codes

PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	

			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3		✖	VLCFA beta-oxidation assays in affected hemizygote fibroblasts showed that VLCFA beta-oxidation is reduced to 20% of normal, indicating that this variant impacts protein function (PMID: 11739809)
PS4		✖	Proband form PMID: 18306728 carries a different initiation codon than the current variant and cannot be counted towards PS4.

PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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