The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000033.4:c.284C>A

Version: 1.0

CA415098539

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: 33aebe52-2cab-4078-98b3-0b2d71af13ee
Approved on: 2026/4/16
Published on: 2026/4/16

HGVS expressions

NM_000033.4:c.284C>A
NC_000023.11:g.153725550C>A
CM000685.2:g.153725550C>A
NC_000023.10:g.152991005C>A
CM000685.1:g.152991005C>A
NC_000023.9:g.152644199C>A
NG_009022.2:g.5683C>A
NG_023231.1:g.4197G>T
ENST00000218104.6:c.284C>A
ENST00000218104.5:c.284C>A
NM_000033.3:c.284C>A

Likely Pathogenic

Met criteria codes 5

PP4 PS4_Supporting PS3_Supporting PM2_Supporting PP1_Moderate

Not Met criteria codes 2

PP3 BP4

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 NM_000033.4:c.284C>A variant in ABCD1 is a missense variant predicted to cause the substitution of alanine by asparagine at amino acid 95 (p.Ala95Asp). At least one patient with this variant was diagnosed with childhood cerebral form adrenoleukodystrophy (C) and elevated VLCFAs, which are specific for adrenoleukodystrophy (PP4, PMID 23651979). This variant has been reported in 1 additional family meeting PP4 phenotype criteria (PS4_Supporting; PMID 23430809). The variant has been reported to segregate with ABCD1 deficiency in 2 affected meioses in addition to the proband (the proband's sister and nephew) in one family (PP1_Moderate; PMID 23430809). This variant is absent from gnomAD v4.1 (PM2_Supporting). Beta-oxidation activity assays in CADDS fibroblasts lacking the ABCD1 gene were completed. They were transfected with the ABCD1 c.284C>A variant, resulting in scarce expression. The C24:0 Beta-oxidation activities

were not recovered, indicating that this variant impacts protein function (PMID: 23430809)(PS3_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic for X-linked adrenoleukodystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen Peroxisomal Disorders VCEP: PP4, PS4_Supporting, PP1_Moderate, PM2_Supporting, PS3_Supporting (ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0)

Met criteria codes

PP4	✔	At least one patient with this variant was diagnosed with childhood cerebral form adrenoleukodystrophy (C) and elevated VLCFAs, which are specific for adrenoleukodystrophy (PP4, PMID 23651979).
PS4_Supporting	✔	This variant has been reported in 1 additional family meeting PP4 phenotype criteria (PS4_Supporting; PMID 23430809).
PS3_Supporting	✔	Beta-oxidation activity assays in CADDS fibroblasts lacking the ABCD1 gene were completed. They were transfected with the ABCD1 c.284C>A variant, resulting in scarce expression. The C24:0 Beta-oxidation activities were not recovered, indicating that this variant impacts protein function (PMID: 23430809)(PS3_Supporting).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP1_Moderate	✔	The variant has been reported to segregate with ABCD1 deficiency in 2 affected meioses in addition to the proband (the proband's sister and nephew) in one family (PP1_Moderate; PMID 23430809).

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.81, which is neither above (≥0.85) nor below (≤0.5) the thresholds set by the Peroxisomal Disorders VCEP predicting a damaging or benign impact on ABCD1 function.
BP4	✖	The results from 2 in silico predictors (REVEL and SpliceAI) do not agree, providing no evidence that correlates with a damaging or benign impact on ABCD1 function. SpliceAI gives a score of 0.03 for donor gain and 0.00 for acceptor loss, donor loss, and acceptor gain, which are below the threshold of ≤0.2, suggesting that the variant has no impact on splicing. However, REVEL gives a score of 0.81, which is neither above (≥0.85) nor below (≤0.5) the thresholds set predicting a damaging or benign impact on ABCD1 function.

Curation History

owing 1 to 1 of 1 rows

ee Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000033.4:c.284C>A	Likely Pathogenic	Adrenoleukodystrophy	2026-04-16	1.0	ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0	ABCD1

owing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.