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(ABCD1):c.310C>T (p.Arg104Cys)

Version: 1.0

CA415098594

1357576 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: d55e71bf-6889-4fe2-9a76-f0c76c730361
Approved on: 2026/4/16
Published on: 2026/4/16

HGVS expressions

NM_000033.4(ABCD1):c.310C>T (p.Arg104Cys)
NM_000033.4:c.310C>T
NC_000023.11:g.153725576C>T
CM000685.2:g.153725576C>T
NC_000023.10:g.152991031C>T
CM000685.1:g.152991031C>T
NC_000023.9:g.152644225C>T
NG_009022.2:g.5709C>T
NG_023231.1:g.4171G>A
ENST00000218104.6:c.310C>T
ENST00000218104.5:c.310C>T
NM_000033.3:c.310C>T

Pathogenic

Met criteria codes 6

PP1_Strong | PS3_Supporting | PS4 | PM2_Supporting | PP3 | PP4

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.310C>T (NM_000033.4) variant in ABCD1 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 104 (p.Arg104Cys). At least one patient with this variant was diagnosed with childhood cerebral from adrenoleukodystrophy and elevated VLCFAs, which are specific for adrenoleukodystrophy (PP4, PMID 26454440). This variant has been reported in 6 additional probands meeting PP4 phenotype criteria (PS4; PMIDs: 8892025, 26454440, 7581394, 37189159, 34826210, 33920672). The variant has been reported to segregate with adrenoleukodystrophy in 4 affected meioses from 1 family (PP1_Strong; PMID 7581394). This variant is absent from gnomAD v4.1 (PM2_Supporting). Western blot shows a reduction of ABCD1 to 35% relative to WT control as well as evidence of

increased degradation by proteases (PMID 21476988; PS3_Supporting). Beta-oxidation assay in ALD patient fibroblasts transfected with the variant showed activity ≤26% of WT (variant transfected cells activity in-line with cells without WT protein transfected), indicating that this variant impacts protein function (PMID 17542813)(PS3_Supporting). The computational predictor REVEL gives a score of 0.943, which is above the ClinGen Peroxisomal Disorders VCEP threshold of ≥0.85, evidence that correlates with impact to ABCD1 function (PP3). In summary, this variant meets the criteria to be classified as pathogenic for X-linked adrenoleukodystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen Peroxisomal Disorders VCEP: PP4, PS4, PP1_Strong, PM2_Supporting, PS3_Supporting, PP3. (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 4 affected meioses from 1 family (PP1_Strong; PMID 7581394).
PS3_Supporting	✔	Western blot shows a reduction of ABCD1 to 35% relative to WT control as well as evidence of increased degradation by proteases (PMID 21476988; PS3_Supporting). Beta-oxidation assay in ALD patient fibroblasts transfected with the variant showed activity ≤26% of WT (variant transfected cells activity in-line with cells without WT protein transfected), indicating that this variant impacts protein function (PMID 17542813)(PS3_Supporting).
PS4	✔	This variant has been reported in 6 additional probands meeting PP4 phenotype criteria (PS4; PMIDs: 8892025, 26454440, 7581394, 37189159, 34826210, 33920672).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.943, which is above the ClinGen Peroxisomal Disorders VCEP threshold of ≥0.85, evidence that correlates with impact to ABCD1 function (PP3).
PP4	✔	At least one patient with this variant was diagnosed with childhood cerebral from adrenoleukodystrophy and elevated VLCFAs, which are specific for adrenoleukodystrophy (PP4, PMID 26454440).

Curation History

howing 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.