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Variant: NM_000033.4(ABCD1):c.1850G>A (p.Arg617His)

Version: 1.0

CA278116

11312 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: 914b35fd-1bb7-4dc2-8a36-9b8f15b5401f
Approved on: 2026/4/16
Published on: 2026/4/16

HGVS expressions

NM_000033.4:c.1850G>A
NM_000033.4(ABCD1):c.1850G>A (p.Arg617His)
NC_000023.11:g.153743056G>A
CM000685.2:g.153743056G>A
NC_000023.10:g.153008510G>A
CM000685.1:g.153008510G>A
NC_000023.9:g.152661704G>A
NG_009022.2:g.23189G>A
ENST00000218104.6:c.1850G>A
ENST00000218104.5:c.1850G>A
NM_000033.3:c.1850G>A

Pathogenic

Met criteria codes 7

PM2_Supporting PP3 PP4 PM1 PS3_Supporting PS4 PS2_Supporting

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.1850G>A variant in ABCD1 is a missense variant predicted to cause substitution of arginine by histidine at amino acid 617 (p.Arg617His). At least one patient with this variant displayed elevated VLCFAs and was diagnosed with the childhood cerebral form of adrenoleukodystrophy, which is specific for adrenoleukodystrophy (PP4; PMID 7581394). This variant has been reported in 7 additional probands meeting PP4 phenotype criteria (PS4; PMIDs 8040304, 21068741, 26454440, 20859061, 30902905). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 1 individual with adrenoleukodystrophy (PS2_Supporting; PMID 8040304). This variant is missing from gnomAD v4.1 genomes (PM2_Supporting). There is a single allele in the exome data but it was flagged by the gnomAD VQSR filter. The computational predictor REVEL gives a score of 0.964, which is above the ClinGen Peroxisomal

Disorders VCEP threshold of ≥0.85, evidence that correlates with impact to ABCD1 function (PP3). This variant resides within the Walker B domain (aa 617 – 641), of ABCD1, a critical functional domain as determined by the ClinGen Peroxisomal Disorders VCEP (PM1). Immunofluorescence assay in p.Arg617His variant transfected X-ALD (163) fibroblasts showed a significant reduction of ABCD1 relative to WT control (PS3_Supporting; PMID 17542813). 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, PM2_Supporting, PP3, PM1, PS2_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

PM2_Supporting	✔	This variant is missing from gnomAD v4.1 genomes (PM2_Supporting). There is a single allele in the exome data but it was flagged by the gnomAD VQSR filter.
PP3	✔	The computational predictor REVEL gives a score of 0.964, 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 displayed elevated VLCFAs and was diagnosed with the childhood cerebral form of adrenoleukodystrophy, which is specific for adrenoleukodystrophy (PP4; PMID 7581394).
PM1	✔	This variant resides within the Walker B domain (aa 617 – 641), of ABCD1, a critical functional domain as determined by the ClinGen Peroxisomal Disorders VCEP (PM1).
PS3_Supporting	✔	Immunofluorescence assay in p.Arg617His variant transfected X-ALD (163) fibroblasts showed a significant reduction of ABCD1 relative to WT control (PS3_Supporting; PMID 17542813).
PS4	✔	This variant has been reported in 7 additional probands meeting PP4 phenotype criteria (PS4; PMIDs 8040304, 21068741, 26454440, 20859061, 30902905).
PS2_Supporting	✔	This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 1 individual with adrenoleukodystrophy (PS2_Supporting; PMID 8040304).

Curation History

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