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.1631A>G (p.Gln544Arg)

Version: 1.0

CA415112066

837244 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: 5e83d125-f8d0-4cb7-aabe-5c099d6f1643
Approved on: 2026/4/17
Published on: 2026/4/17

HGVS expressions

NM_000033.4(ABCD1):c.1631A>G (p.Gln544Arg)
NM_000033.4:c.1631A>G
NC_000023.11:g.153740234A>G
CM000685.2:g.153740234A>G
NC_000023.10:g.153005688A>G
CM000685.1:g.153005688A>G
NC_000023.9:g.152658882A>G
NG_009022.2:g.20367A>G
ENST00000218104.6:c.1631A>G
ENST00000218104.5:c.1631A>G
ENST00000443684.2:n.634A>G
NM_000033.3:c.1631A>G

Likely Pathogenic

Met criteria codes 5

PS3_Supporting PS4 PM2_Supporting PP3 PP4

Not Met criteria codes 1

BS3

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.1631A>G (p.Gln544Arg) variant in ABCD1 is a missense variant predicted to cause substitution of glutamine by arginine at amino acid 544 (p.Gln544Arg). At least one patient with this variant displayed rapid progression of inflammatory white matter demyelination in childhood and abnormal very long chain fatty acid testing, which is highly specific for adrenoleukodystrophy (PP4, PMID:10190819). This variant has been reported in 5 additional probands meeting PP4 phenotype criteria (PS4; PMIDs 21068741, 32632637, 10190819, 20661612). This variant is absent from gnomAD v2.1.1, v3.1.2 and v4.1.0 (PM2_Supporting). Beta-oxidation assay in X-ALD fibroblasts (163T) showed that the beta-oxidation activity of the variant protein is approximately 1.6% of wild type ABCD1, indicating that this variant

has impact protein function (PMID:17542813)(PS3_Supporting). The computational predictor REVEL gives a score of 0.958, which is above the threshold of 0.85, evidence that correlates with impact to ABCD1 function (PP3). 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: PS3_Supporting, PP4, PS4, PM2_Supporting, PP3 (ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0)

Met criteria codes

PS3_Supporting	✔	Beta-oxidation assay in X-ALD fibroblasts (163T) showed that the beta-oxidation activity of the variant protein is approximately 1.6% of wild type ABCD1, indicating that this variant has impact protein function (PMID:17542813) (PS3_Supporting).
PS4	✔	This variant has been reported in 5 additional probands meeting PP4 phenotype criteria (PS4; PMIDs 21068741, 32632637, 10190819, 20661612).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1, v3.1.2 and v4.1.0 (PM2_Supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.958, which is above the threshold of 0.85, evidence that correlates with impact to ABCD1 function (PP3).
PP4	✔	At least one patient with this variant displayed rapid progression of inflammatory white matter demyelination in childhood and abnormal very long chain fatty acid testing, which is highly specific for adrenoleukodystrophy (PP4, PMID:10190819).

Not Met criteria codes

BS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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