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Variant: NM_000033.4(ABCD1):c.1A>G (p.Met1Val)

Version: 1.0

CA415097154

851448 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: c5c33107-d069-416c-ae57-e40dd95e3c99
Approved on: 2026/4/17
Published on: 2026/4/17

HGVS expressions

NM_000033.4:c.1A>G
NM_000033.4(ABCD1):c.1A>G (p.Met1Val)
NC_000023.11:g.153725267A>G
CM000685.2:g.153725267A>G
NC_000023.10:g.152990722A>G
CM000685.1:g.152990722A>G
NC_000023.9:g.152643916A>G
NG_009022.2:g.5400A>G
NG_023231.1:g.4480T>C
ENST00000218104.6:c.1A>G
ENST00000218104.5:c.1A>G
NM_000033.3:c.1A>G

Likely Pathogenic

Met criteria codes 5

PS3_Supporting PVS1_Moderate PM2_Supporting PS4 PP4

Not Met criteria codes 2

BP4 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.1A>G (p.Met1Val) variant in ABCD1 may cause a truncated or absent protein by altering the start codon of the coding sequence (PVS1_Moderate). At least one patient with this variant displayed a primary adrenal insufficiency and increased plasma VLCFAs, which is highly specific for X-linked adrenoleukodystrophy (PP4; PMID:22176151). This variant has been reported in six more male probands meeting with a primary adrenal insufficiency and increased VLCFA ratios (PS4; PMID:34946879). This variant is absent from gnomAD v2.1.1, v3.1.2 and v4.1.0 (PM2_Supporting). Immunoblotting in transformed clonal cell lines showed severely reduced expression indicating that this variant impacts protein function. Beta-oxidation assay in transformed clonal cell lines showed the variant activity to be

about 19.6% of wild type activity indicating that this variant impacts protein function (PMID:27067449, 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: PVS1_Moderate, PS4, PP4, 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

PS3_Supporting	✔	Immunoblotting in transformed clonal cell lines showed severely reduced expression indicating that this variant impacts protein function. Beta-oxidation assay in transformed clonal cell lines showed the variant activity to be about 19.6% of wild type activity indicating that this variant impacts protein function (PMID:27067449, PS3_Supporting).
PVS1_Moderate	✔	The c.1A>G (p.Met1Val) variant in ABCD1 may cause a truncated or absent protein by altering the start codon of the coding sequence (PVS1_Moderate).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1, v3.1.2 and v4.1.0 (PM2_Supporting).
PS4	✔	This variant has been reported in six more male probands meeting with a primary adrenal insufficiency and increased VLCFA ratios (PS4; PMID:34946879).
PP4	✔	At least one patient with this variant displayed a primary adrenal insufficiency and increased plasma VLCFAs, which is highly specific for X-linked adrenoleukodystrophy (PP4; PMID:22176151).

Not Met criteria codes

BP4	✖	REVEL = 0.591
PP3	✖	REVEL = 0.591

Curation History

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