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Variant: NM_000033.4(ABCD1):c.900+2T>C

Version: 1.0

CA415100411

1172887 (ClinVar)

Gene: ABCD1 (HGNC:215)
Condition: adrenoleukodystrophy (MONDO:0018544)
Inheritance Mode: X-linked inheritance
UUID: 3eafa513-947d-4667-aa9d-21bc2fbf9158
Approved on: 2026/4/16
Published on: 2026/4/16

HGVS expressions

NM_000033.4:c.900+2T>C
NM_000033.4(ABCD1):c.900+2T>C
NC_000023.11:g.153726168T>C
CM000685.2:g.153726168T>C
NC_000023.10:g.152991623T>C
CM000685.1:g.152991623T>C
NC_000023.9:g.152644817T>C
NG_009022.2:g.6301T>C
NG_023231.1:g.3579A>G
ENST00000218104.6:c.900+2T>C
ENST00000218104.5:c.900+2T>C
ENST00000370129.4:c.345+2T>C
NM_000033.3:c.900+2T>C

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PM2_Supporting PS1_Moderate

Not Met criteria codes 18

PP1 PP3 PP4 PM6 BA1 PM1 PM5 PM4 BS1 BS4 BS3 BS2 PS2 PS3 PS4 BP5 BP4 BP2

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.900+2T>C variant in ABCD1 occurs within the canonical splice donor site (+2) of intron 1. It is predicted to cause skipping of biologically-relevant-exon 1, resulting in an in-frame deletion (removes amino acids 1-300). However, it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong). A different single nucleotide variant (c.900+2T>A) in the same canonical splice dinucleotide, expected to cause skipping of exon 1 (PMID 36180238), is classified as likely pathogenic for X-linked

adrenoleukodystrophy by the ClinGen Peroxisomal Disorders VCEP (PS1_Moderate). This variant is absent from gnomADv4.1, gnomAD v3.1.2 and v.2.1.1 and therefore meets the criteria for PM2 Supporting (PM2_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 VCEP: PVS1_Strong, PS1_Moderate, PM2_Supporting. (ClinGen Peroxisomal Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCD1 Version 1.0.0)

Met criteria codes

PVS1_Strong	✔	The NM_000033.4:c.900+2T>G variant in ABCD1 occurs within the canonical splice donor site (+2) of intron 1. It is predicted to cause skipping of biologically-relevant-exon 1, resulting in an in-frame deletion (removes amino acids 1-300). However, it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong).
PM2_Supporting	✔	not in gnomAD
PS1_Moderate	✔	A different single nucleotide variant (c.900+2T>A) in the same canonical splice dinucleotide, expected to cause skipping of exon 1 (PMID 36180238), is classified as likely pathogenic for X-linked adrenoleukodystrophy by the ClinGen Peroxisomal Disorders VCEP (PS1_Moderate).

Not Met criteria codes

PP1	✖	only one known affected patient
PP3	✖	no computational evidence
PP4	✖	only one known patient and no actual data on them/family
PM6	✖	not confirmed (no studies)
BA1	✖	not in gnomAD
PM1	✖	already counting PVS1
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	not in gnomAD
BS4	✖	no studies
BS3	✖	no studies

BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No clinical information, no confirmed de novo
PS3		✖	No studies
PS4		✖	No frequencies reported
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	unknown/no studies

Curation History

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