

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

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HGVS expressions

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

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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 PS1_Moderate

PM2_Supporting

Not Met criteria codes **18**

BA1 BS1 BS4 BS3 BS2 BP5

BP4 BP2 PS2 PS3 PS4 PP1

PP3 PP4 PM1 PM5 PM4

PM6

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).
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).
PM2_Supporting			not in gnomAD

Not Met criteria codes

BA1			not in gnomAD
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
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
PS2			No clinical information, no confirmed de novo
PS3			No studies

PS4			No frequencies reported
PP1			only one known affected patient
PP3			no computational evidence
PP4			only one known patient and no actual data on them/family
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
PM6			not confirmed (no studies)

Curation History 		
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