

Variant: NR_136160.2:n.94T>G

Version: 1.0

CA409122633 [↗](#)

2709658 (ClinVar) [↗](#)

Gene: ADA ([HGNC:100](#))

Condition: severe combined immunodeficiency ([MONDO:0015974](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: c188c8c2-bf2f-422a-9a17-d5193d2ed908

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HGVS expressions

NR_136160.2:n.94T>G

NC_000020.11:g.44651606A>C
CM000682.2:g.44651606A>C
NC_000020.10:g.43280247A>C
CM000682.1:g.43280247A>C
NC_000020.9:g.42713661A>C
NG_007385.1:g.5130T>G
ENST00000492931.6:n.93T>G
ENST00000536076.2:c.-121+296T>G
ENST00000536532.6:c.2T>G
ENST00000537820.2:c.2T>G
ENST00000539235.6:c.2T>G
ENST00000695889.1:c.2T>G
ENST00000695891.1:c.2T>G
ENST00000695949.1:c.2T>G
ENST00000695957.1:c.2T>G
ENST00000695991.1:c.2T>G
ENST00000695992.1:c.2T>G
ENST00000695993.1:c.2T>G
ENST00000695994.1:c.2T>G
ENST00000695995.1:c.2T>G
ENST00000695996.1:n.73T>G
ENST00000695997.1:n.73T>G
ENST00000696003.1:n.94T>G
ENST00000696004.1:n.94T>G
ENST00000696006.1:c.2T>G
ENST00000696009.1:n.113T>G
ENST00000696010.1:n.115T>G
ENST00000696017.1:c.2T>G
ENST00000696034.1:c.2T>G
ENST00000696038.1:c.2T>G
ENST00000696039.1:n.321+296T>G
ENST00000696058.1:c.2T>G
ENST00000696059.1:c.2T>G
ENST00000696060.1:c.2T>G
ENST00000696061.1:c.2T>G
ENST00000696062.1:c.96+494T>G

ENST00000696063.1:c.2T>G
ENST00000696064.1:c.-118+296T>G
ENST00000696065.1:c.-121+296T>G
ENST00000696075.1:c.2T>G
ENST00000696076.1:c.2T>G
ENST00000696077.1:c.2T>G
ENST00000696078.1:c.2T>G
ENST00000696079.1:c.2T>G
ENST00000696080.1:c.2T>G
ENST00000696084.1:n.103T>G
ENST00000696104.1:c.2T>G
ENST00000696105.1:c.2T>G
ENST00000372874.9:c.2T>G
ENST00000372874.8:c.2T>G
ENST00000492931.5:n.86T>G
ENST00000535573.1:n.332+296T>G
ENST00000536076.1:n.213+296T>G
ENST00000536532.5:c.2T>G
ENST00000537820.1:c.2T>G
ENST00000539235.5:c.2T>G
ENST00000545776.5:n.56T>G
NM_000022.2:c.2T>G
NM_000022.3:c.2T>G
NM_001322050.1:c.-288T>G
NM_001322051.1:c.2T>G
NR_136160.1:n.153T>G
NM_000022.4:c.2T>G
NM_001322050.2:c.-288T>G
NM_001322051.2:c.2T>G

Uncertain Significance

Met criteria codes 3

PVS1_Moderate

PM2_Supporting

PS3_Moderate

Not Met criteria codes 2

PM5

PS1

Evidence Links 0

Expert Panel

Severe Combined Immunodeficiency Disease VCEP

Criteria Specification Information

Criteria Specification: ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ADA Version 2.1.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The NM_000022.4(ADA):c.2T>G is a missense variant predicted to cause substitution of Methionine by Arginine at amino acid 1 (p.Met1Arg). This sequence change affects the initiator methionine of the ADA mRNA. The next possible initiation codon is at codon 52. This variant is absent from gnomAD v4.1.0, good coverage (PM2_supporting). The NM_000022.4:c.2T>G variant in ADA may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region

of the protein (PVS1_Moderate). ADA enzyme activity assay in E. coli S3834 showed 0.01% of wild-type activity for the p.Met1Arg variant, indicating severely reduced protein function consistent with loss of function (PS3_Moderate). In summary, this variant meets the criteria to be classified as uncertain significance for SCID based on the ACMG/AMP criteria applied, as specified by the ClinGen ClinGen SCID-VCEP: PM2_supporting, PVS1_moderate, PS3_moderate. (VCEP specifications version 2.1.0).

Met criteria codes

PVS1_Moderate			The NM_000022.4:c.2T>G (p.Met1?) variant in ADA may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1_Moderate).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 good coverage (PM2_supporting)
PS3_Moderate			ADA enzyme activity assay in E. coli S3834 showed 0.01% of wild-type activity for the p.Met1Arg variant, indicating severely reduced protein function consistent with loss of function (PS3_Moderate).

Not Met criteria codes

PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



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