

Variant: NM_000022.4(ADA):c.899T>G (p.Phe300Cys)

Version: 1.0

CA9871470 [↗](#)

897016 (ClinVar) [↗](#)

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

Condition: adenosine deaminase deficiency ([MONDO:0007064](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 3d04b3e3-b3c9-4a74-990c-d85b6725a0fa

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HGVS expressions

NM_000022.4(ADA):c.899T>G (p.Phe300Cys)

NM_000022.4:c.899T>G

NC_000020.11:g.44621094A>C

CM000682.2:g.44621094A>C

NC_000020.10:g.43249735A>C

CM000682.1:g.43249735A>C

NC_000020.9:g.42683149A>C

NG_007385.1:g.35642T>G

ENST00000492931.6:n.1066T>G

ENST00000536076.2:c.746T>G

ENST00000536532.6:c.*42T>G

ENST00000537820.2:c.827T>G

ENST00000539235.6:c.*283T>G

ENST00000695889.1:c.374T>G

ENST00000695890.1:n.4394T>G

ENST00000695891.1:c.439T>G

ENST00000695927.1:c.977T>G

ENST00000695949.1:c.824T>G

ENST00000695956.1:c.54T>G

ENST00000695957.1:c.*390T>G

ENST00000695991.1:c.437T>G

ENST00000695992.1:c.*42T>G

ENST00000695993.1:c.899T>G

ENST00000695994.1:c.*42T>G

ENST00000695995.1:c.509T>G

ENST00000695996.1:n.981T>G

ENST00000696003.1:n.2683T>G

ENST00000696004.1:n.1067T>G

ENST00000696005.1:c.349T>G

ENST00000696006.1:c.*42T>G

ENST00000696007.1:c.826T>G

ENST00000696008.1:n.3253T>G

ENST00000696017.1:c.896T>G

ENST00000696034.1:c.*42T>G

ENST00000696035.1:n.1085T>G

ENST00000696036.1:n.1600T>G

ENST00000696037.1:n.2576T>G

ENST00000696038.1:c.*656T>G
ENST00000696039.1:n.1263T>G
ENST00000696058.1:c.896T>G
ENST00000696059.1:c.*844T>G
ENST00000696060.1:c.968T>G
ENST00000696061.1:c.896T>G
ENST00000696062.1:c.962T>G
ENST00000696063.1:c.974T>G
ENST00000696064.1:c.746T>G
ENST00000696065.1:c.221T>G
ENST00000696072.1:n.254T>G
ENST00000696073.1:n.1210T>G
ENST00000696074.1:n.450T>G
ENST00000696075.1:c.*869T>G
ENST00000696076.1:c.968T>G
ENST00000696077.1:c.893T>G
ENST00000696078.1:c.896T>G
ENST00000696079.1:c.896T>G
ENST00000696080.1:c.899T>G
ENST00000696081.1:n.1018T>G
ENST00000696082.1:c.974T>G
ENST00000696083.1:n.1856T>G
ENST00000696084.1:n.1076T>G
ENST00000696104.1:c.583T>G
ENST00000372874.9:c.899T>G
ENST00000372874.8:c.899T>G
ENST00000372887.5:c.152-2839A>C
ENST00000464097.5:n.649T>G
ENST00000492931.5:n.1059T>G
ENST00000536532.5:c.*42T>G
ENST00000537820.1:c.827T>G
ENST00000539235.5:c.*283T>G
NM_000022.2:c.899T>G
NM_000022.3:c.899T>G
NM_001322050.1:c.494T>G
NM_001322051.1:c.827T>G
NR_136160.1:n.985T>G
NM_001322050.2:c.494T>G
NM_001322051.2:c.827T>G
NR_136160.2:n.926T>G

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 5

BS3

BS2

PM5

PS1

PS3

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 1.0.0

Criteria Specification Approval History

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The c.899T>G (NM_000022.4) variant in ADA is a missense variant predicted to cause substitution of Phenylalanine by Cysteine at amino acid 300 (p.Phe300Cys). The filtering allele frequency (the upper threshold of the 95% CI of 64/1180048) of the c.899T>G variant in ADA is 0.00004346 for European (non-Finnish) chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). No homozygotes have been observed in gnomAD. To our knowledge, this variant has not been reported in the literature in individuals affected with ADA-related conditions or in functional studies. Due to insufficient evidence, this variant is classified as a variant of uncertain significance for autosomal recessive SCID based on ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP (specification version 1.0): PM2_Supporting.

Met criteria codes

PM2_Supporting			The filtering allele frequency (the upper threshold of the 95% CI of 64/1180048) of the c.899T>G variant in ADA is 0.00004346 for European (non-Finnish) chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). No homozygotes have been observed in gnomAD.
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Not Met criteria codes

BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

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