

Variant: NM_000022.4(ADA):c.935A>G (p.Lys312Arg)

Version: 1.0

CA9871464 [↗](#)

1507601 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: ec440f51-ed74-4a57-9e84-f4c2fb2dce19

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HGVS expressions

NM_000022.4(ADA):c.935A>G (p.Lys312Arg)

NM_000022.4:c.935A>G

NC_000020.11:g.44621058T>C

CM000682.2:g.44621058T>C

NC_000020.10:g.43249699T>C

CM000682.1:g.43249699T>C

NC_000020.9:g.42683113T>C

NG_007385.1:g.35678A>G

ENST00000492931.6:n.1102A>G

ENST00000536076.2:c.782A>G

ENST00000536532.6:c.*78A>G

ENST00000537820.2:c.863A>G

ENST00000539235.6:c.*319A>G

ENST00000695889.1:c.410A>G

ENST00000695890.1:n.4430A>G

ENST00000695891.1:c.475A>G

ENST00000695927.1:c.1013A>G

ENST00000695949.1:c.860A>G

ENST00000695956.1:c.90A>G

ENST00000695957.1:c.*426A>G

ENST00000695991.1:c.473A>G

ENST00000695992.1:c.*78A>G

ENST00000695993.1:c.935A>G

ENST00000695994.1:c.*78A>G

ENST00000695995.1:c.545A>G

ENST00000695996.1:n.1017A>G

ENST00000696003.1:n.2719A>G

ENST00000696004.1:n.1103A>G

ENST00000696005.1:c.385A>G

ENST00000696006.1:c.*78A>G

ENST00000696007.1:c.862A>G

ENST00000696008.1:n.3289A>G

ENST00000696017.1:c.932A>G

ENST00000696034.1:c.*78A>G

ENST00000696035.1:n.1121A>G

ENST00000696036.1:n.1636A>G

ENST00000696037.1:n.2612A>G

	ENST00000696038.1:c.*692A>G ENST00000696039.1:n.1299A>G ENST00000696058.1:c.932A>G ENST00000696059.1:c.*880A>G ENST00000696060.1:c.1004A>G ENST00000696061.1:c.932A>G ENST00000696062.1:c.998A>G ENST00000696063.1:c.1010A>G ENST00000696064.1:c.782A>G ENST00000696065.1:c.257A>G ENST00000696072.1:n.290A>G ENST00000696073.1:n.1246A>G ENST00000696074.1:n.486A>G ENST00000696075.1:c.*905A>G ENST00000696076.1:c.1004A>G ENST00000696077.1:c.929A>G ENST00000696078.1:c.932A>G ENST00000696079.1:c.932A>G ENST00000696080.1:c.935A>G ENST00000696081.1:n.1054A>G ENST00000696082.1:c.1010A>G ENST00000696083.1:n.1892A>G ENST00000696084.1:n.1112A>G ENST00000696104.1:c.*4A>G ENST00000372874.9:c.935A>G ENST00000372874.8:c.935A>G ENST00000372887.5:c.152-2875T>C ENST00000464097.5:n.685A>G ENST00000492931.5:n.1095A>G ENST00000536532.5:c.*78A>G ENST00000537820.1:c.863A>G ENST00000539235.5:c.*319A>G NM_000022.2:c.935A>G NM_000022.3:c.935A>G NM_001322050.1:c.530A>G NM_001322051.1:c.863A>G NR_136160.1:n.1021A>G NM_001322050.2:c.530A>G NM_001322051.2:c.863A>G NR_136160.2:n.962A>G
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Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 1

PM5

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.935A>G (NM_000022.4) variant in ADA is a missense variant predicted to cause substitution of Lysine by Arginine at amino acid 312 (p.Lys312Arg). The filtering allele frequency (the upper threshold of the 95% CI of (4/418132 alleles) of the c.935A>G variant in ADA is 0.000003240 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. Another missense variant [c.934A>C, p.Lys312Gln] in the same codon has been reported; however, the ClinGen SCID VCEP classified this variant as VUS (PM5 not met). 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 (4/418132 alleles) of the c.935A>G variant in ADA is 0.000003240 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

PM5			Another missense variant [c.934A>C, p.Lys312Gln] in the same codon has been reported; However, this variant was classified as VUS by the ClinGen SCID VCEP (PM5 not met).
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Curation History [↗](#)



 

 

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