

Variant: NM_000022.4(ADA):c.632G>A (p.Arg211His)

Version: 1.1

CA252000 [↗](#)

1957 (ClinVar) [↗](#)

Gene: ADA ([HGNC:100](#))
Condition: adenosine deaminase deficiency ([MONDO:0007064](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: 4c664ec8-5d63-46a5-a3d1-142655c6aa1c
Approved on: 2026/2/17
Published on: 2026/2/17

HGVS expressions

NM_000022.4(ADA):c.632G>A (p.Arg211His)
NM_000022.4:c.632G>A
NC_000020.11:g.44623053C>T
CM000682.2:g.44623053C>T
NC_000020.10:g.43251694C>T
CM000682.1:g.43251694C>T
NC_000020.9:g.42685108C>T
NG_007385.1:g.33683G>A
ENST00000492931.6:n.723G>A
ENST00000536076.2:c.479G>A
ENST00000536532.6:c.632G>A
ENST00000537820.2:c.607-123G>A
ENST00000539235.6:c.*16G>A
ENST00000695889.1:c.219-123G>A
ENST00000695890.1:n.2435G>A
ENST00000695891.1:c.219-123G>A
ENST00000695927.1:c.710G>A
ENST00000695949.1:c.604-123G>A
ENST00000695957.1:c.*123G>A
ENST00000695991.1:c.217-123G>A
ENST00000695992.1:c.632G>A
ENST00000695993.1:c.632G>A
ENST00000695994.1:c.632G>A
ENST00000695995.1:c.242G>A
ENST00000695996.1:n.703G>A
ENST00000696003.1:n.724G>A
ENST00000696004.1:n.724G>A
ENST00000696005.1:c.129-123G>A
ENST00000696006.1:c.607-123G>A
ENST00000696007.1:c.483G>A
ENST00000696008.1:n.2910G>A
ENST00000696017.1:c.629G>A
ENST00000696034.1:c.632G>A
ENST00000696035.1:n.742G>A
ENST00000696036.1:n.1322G>A
ENST00000696037.1:n.2309G>A
ENST00000696038.1:c.*378G>A

	ENST00000696039.1:n.920G>A ENST00000696058.1:c.629G>A ENST00000696059.1:c.*577G>A ENST00000696060.1:c.701G>A ENST00000696061.1:c.629G>A ENST00000696062.1:c.695G>A ENST00000696063.1:c.707G>A ENST00000696064.1:c.479G>A ENST00000696065.1:c.66-123G>A ENST00000696073.1:n.867G>A ENST00000696074.1:n.248G>A ENST00000696075.1:c.*602G>A ENST00000696076.1:c.701G>A ENST00000696077.1:c.626G>A ENST00000696078.1:c.629G>A ENST00000696079.1:c.629G>A ENST00000696080.1:c.632G>A ENST00000696081.1:n.751G>A ENST00000696082.1:c.707G>A ENST00000696083.1:n.1513G>A ENST00000696084.1:n.733G>A ENST00000696104.1:c.363-123G>A ENST00000696105.1:c.*173G>A ENST00000372874.9:c.632G>A ENST00000372874.8:c.632G>A ENST00000372887.5:c.152-880C>T ENST00000464097.5:n.306G>A ENST00000492931.5:n.716G>A ENST00000536532.5:c.632G>A ENST00000537820.1:c.607-123G>A ENST00000539235.5:c.*16G>A NM_000022.2:c.632G>A NM_000022.3:c.632G>A NM_001322050.1:c.227G>A NM_001322051.1:c.607-123G>A NR_136160.1:n.783G>A NM_001322050.2:c.227G>A NM_001322051.2:c.607-123G>A NR_136160.2:n.724G>A
--	---

Pathogenic

Met criteria codes 5

- PP1_Strong
- PP4_Moderate
- PM2_Supporting
- PS3_Moderate
- PM3_Strong

Not Met criteria codes 1

- 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 1.0.0
- [Criteria Specification Approval History](#)
- [Criteria Specifications for this VCEP](#)

Severe Combined Immunodeficiency Disease VCEP

The NM_000022.4:c.632G>A variant in ADA is a missense variant predicted to cause substitution of arginine by histidine at amino acid 211 (p.Arg211His). The filtering allele frequency (the upper threshold of the 95% CI of 10/35432) of the c.632G>A variant in ADA is 0.0001565 for Latino/Admixed American chromosomes by gnomAD v.2.1.1, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) and therefore meets this criterion (PM2_Supporting). Total Expressed ADA Activity in SØ3834 in E. coli showed the values: Mean +- SD = 30.4 +- 35.8 (3.0-134.2)[nmol/h/mg protein] and the following percent of Wild Type (Range) = 0.012 - 0.014 (0.001-0.051), belonging to group I of Arredondo-Vega classification, indicating that this variant impacts protein function (PMID: 9758612, PS3_moderate). This variant has been detected in 22 individuals with SCID. Of those individuals, one was a heterozygous compound with c.95+1G>A (variant classified pathogenic according to the SCID VCEP specifications). The trans phase of the variants was confirmed by parental testing (1pt; PMID 9414266). Four individuals were with this variant, and a variant that has not been curated by the SCID VCEP (p.A179D, PMID 26684479; p.R101Q, PMID 16973956; p.Y201*, PMID 26255240, patient #46; p.L107P, PMID 19179314, patient #2) (0pt - These variants will not be curated now because the pathogenic level was already reached). Seventeen individuals were homozygous for the variant (maximum 1pt; PMID 27129325, 20460637, 26376800, 19179314, 16276484, 9758612). 2pts in total, PM3_Strong is met. At least one patient with this variant displayed: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome (0.5pt) + Reduced ADA enzyme activity in patient cells (1pt) + Increased dAdo nucleotides (dATP or dAXP) in pretreatment erythrocytes (2pt) + ADA-SCID phenotype corrected by ADA gene therapy (1pt), in a total of 4.5 points, which is highly specific for SCID (PP4_Moderate; PMID: 9414266). The variant has been reported to segregate with SCID in 4 affected family members from 2 families (LOD score 2.41; PP1_Strong; PMID 20460637, 26376800). In summary, this variant meets the criteria to be classified as pathogenic for SCID. ACMG/AMP criteria applied, as specified by the ClinGen SCID-VCEP: PP4_Moderate, PM3_Strong, PP1_Strong, PM2_Supporting, PS3_Moderate. (VCEP specifications version 1).

Met criteria codes

PP1_Strong			The variant has been reported to segregate with SCID in 4 affected family members from 2 families (LOD score 2.41; PP1_Strong; PMID 20460637, 26376800).
PP4_Moderate			At least one patient with this variant displayed: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome (0.5pt) + Reduced ADA enzyme activity in patient cells (1pt) + Increased dAdo nucleotides (dATP or dAXP) in pretreatment erythrocytes (2pt) + ADA-SCID phenotype corrected by ADA gene therapy (1pt), in a total of 4.5 points, which is highly specific for SCID (PP4_Moderate; PMID: 9414266).
PM2_Supporting			The filtering allele frequency (the upper threshold of the 95% CI of 10/35432) of the c.632G>A variant in ADA is 0.0001565 for Latino/Admixed American chromosomes by gnomAD v.2.1.1, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) and therefore meets this criterion (PM2_Supporting).
PS3_Moderate			Total Expressed ADA Activity in SØ3834 in E. coli showed the values: Mean +- SD = 30.4 +- 35.8 (3.0-134.2) [nmol/h/mg protein] and the following percent of Wild Type (Range) = 0.012 - 0.014 (0.001-0.051), belonging to group I of Arredondo-Vega classification, indicating that this variant impacts protein function (PMID: 9758612, PS3_moderate).
PM3_Strong			This variant has been detected in 22 individuals with SCID. Of those individuals, one was a heterozygous compound with c.95+1G>A (variant classified pathogenic according to the SCID VCEP specifications). The trans phase of the variants was confirmed by parental testing (1pt; PMID 9414266). Four individuals were with this variant, and a variant that has not been curated by the SCID VCEP (p.A179D, PMID 26684479; p.R101Q, PMID 16973956; p.Y201*, PMID 26255240, patient #46; p.L107P, PMID 19179314, patient #2) (0pt - These variants will not be curated now

because the pathogenic level was already reached). Seventeen individuals were homozygous for the variant (maximum 1pt; PMID 27129325, 20460637, 26376800, 19179314, 16276484, 9758612). 2pts in total, PM3_Strong is met.

Not Met criteria codes

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

Curation History



 ▾

 ▾

Showing 1 to 2 of 2 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.