The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000022.4(ADA):c.631C>T (p.Arg211Cys)

Version: 1.0

CA115285

1966 (ClinVar)

Gene: ADA (HGNC:100)
Condition: adenosine deaminase deficiency (MONDO:0007064)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4f92adc5-3431-4f25-8298-d4cd9bfea5a6
Approved on: 2024/1/10
Published on: 2024/1/10

HGVS expressions

NM_000022.4:c.631C>T
NM_000022.4(ADA):c.631C>T (p.Arg211Cys)
NC_000020.11:g.44623054G>A
CM000682.2:g.44623054G>A
NC_000020.10:g.43251695G>A
CM000682.1:g.43251695G>A
NC_000020.9:g.42685109G>A
NG_007385.1:g.33682C>T
ENST00000492931.6:n.722C>T
ENST00000536076.2:c.478C>T
ENST00000536532.6:c.631C>T
ENST00000537820.2:c.607-124C>T
ENST00000539235.6:c.*15C>T
ENST00000695889.1:c.219-124C>T
ENST00000695890.1:n.2434C>T
ENST00000695891.1:c.219-124C>T
ENST00000695927.1:c.709C>T
ENST00000695949.1:c.604-124C>T
ENST00000695957.1:c.*122C>T
ENST00000695991.1:c.217-124C>T
ENST00000695992.1:c.631C>T
ENST00000695993.1:c.631C>T
ENST00000695994.1:c.631C>T
ENST00000695995.1:c.241C>T
ENST00000695996.1:n.702C>T
ENST00000696003.1:n.723C>T
ENST00000696004.1:n.723C>T
ENST00000696005.1:c.129-124C>T
ENST00000696006.1:c.607-124C>T
ENST00000696007.1:c.482C>T
ENST00000696008.1:n.2909C>T
ENST00000696017.1:c.628C>T
ENST00000696034.1:c.631C>T
ENST00000696035.1:n.741C>T
ENST00000696036.1:n.1321C>T
ENST00000696037.1:n.2308C>T
ENST00000696038.1:c.*377C>T

ENST00000696039.1:n.919C>T
ENST00000696058.1:c.628C>T
ENST00000696059.1:c.*576C>T
ENST00000696060.1:c.700C>T
ENST00000696061.1:c.628C>T
ENST00000696062.1:c.694C>T
ENST00000696063.1:c.706C>T
ENST00000696064.1:c.478C>T
ENST00000696065.1:c.66-124C>T
ENST00000696073.1:n.866C>T
ENST00000696074.1:n.247C>T
ENST00000696075.1:c.*601C>T
ENST00000696076.1:c.700C>T
ENST00000696077.1:c.625C>T
ENST00000696078.1:c.628C>T
ENST00000696079.1:c.628C>T
ENST00000696080.1:c.631C>T
ENST00000696081.1:n.750C>T
ENST00000696082.1:c.706C>T
ENST00000696083.1:n.1512C>T
ENST00000696084.1:n.732C>T
ENST00000696104.1:c.363-124C>T
ENST00000696105.1:c.*172C>T
ENST00000372874.9:c.631C>T
ENST00000372874.8:c.631C>T
ENST00000372887.5:c.152-879G>A
ENST00000464097.5:n.305C>T
ENST00000492931.5:n.715C>T
ENST00000536532.5:c.631C>T
ENST00000537820.1:c.607-124C>T
ENST00000539235.5:c.*15C>T
NM_000022.2:c.631C>T
NM_000022.3:c.631C>T
NM_001322050.1:c.226C>T
NM_001322051.1:c.607-124C>T
NR_136160.1:n.782C>T
NM_001322050.2:c.226C>T
NM_001322051.2:c.607-124C>T
NR_136160.2:n.723C>T

Likely Pathogenic

Met criteria codes 3

PM3 PM5 PP1_Moderate

Not Met criteria codes 1

PM2

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**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000022.4:c.631C>T is a missense variant predicted to cause substitution of Arginine by Cysteine at amino acid 211 (p. Arg211Cys). The highest population minor allele frequency in gnomAD v4 is 0.0005167 (31/60000) in Admixed American population (PM2_Supporting, BS1, and BA1 are not met). The variant has been reported to segregate with SCID in 2 affected family members from 1 family (PP1_moderate; PMID :8051429). Patient was found heterozygous for R211C & L107P which is classified as likely pathogenic by SCID VCEP (1 pt.) (PM3) (PMID: 2166947).Another missense variant [c.632G>A, p.Arg211His)] in the same codon has been classified as pathogenic for SCID by the ClinGen SCID VCEP (PM5). In summary, this variant meets the criteria to be classified as a Likely Pathogenic variant for autosomal recessive severe combined immunodeficiency due to ADA deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PP1_moderate,PM3,PM5(VCEP specifications version 1).

Met criteria codes

PM3	✔	Patient was found heterozygous for R211C & L107P which is classified as likely pathogenic by SCID VCEP (1 pt.) (PM3) (PMID: 2166947)
PM5	✔	Another missense variant [c.632G>A, p.Arg211His)] in the same codon has been classified as pathogenic for SCID by the ClinGen SCID VCEP (PM5).
PP1_Moderate	✔	The variant has been reported to segregate with SCID in 2 affected family members from 1 family (PP1_moderate; PMID: 8051429)

Not Met criteria codes

PM2	✖	The highest population minor allele frequency in gnomAD v4 is 0.0005167 (31/60000) in Admixed American population. (PM2_Supporting, BS1, and BA1 are not met)

Curation History

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