

Variant: NM_000022.4(ADA):c.396dup (p.Val133fs)

Version: 1.0

CA658824668 [↗](#)

550821 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4ab2445c-e8c4-479d-87cb-de2f90731ef3

Approved on: 2024/1/17

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HGVS expressions

NM_000022.4:c.396dup

NM_000022.4(ADA):c.396dup (p.Val133fs)

NC_000020.11:g.44625651dup

CM000682.2:g.44625651dup

NC_000020.10:g.43254292dup

CM000682.1:g.43254292dup

NC_000020.9:g.42687706dup

NG_007385.1:g.31085dup

ENST00000492931.6:n.487dup

ENST00000536076.2:c.243dup

ENST00000536532.6:c.396dup

ENST00000537820.2:c.396dup

ENST00000539235.6:c.219-2573dup

ENST00000695889.1:c.219-2721dup

ENST00000695890.1:n.2199dup

ENST00000695891.1:c.219-2721dup

ENST00000695927.1:c.474dup

ENST00000695949.1:c.393dup

ENST00000695957.1:c.362+805dup

ENST00000695991.1:c.217-2721dup

ENST00000695992.1:c.396dup

ENST00000695993.1:c.396dup

ENST00000695994.1:c.396dup

ENST00000695995.1:c.217-2573dup

ENST00000695996.1:n.467dup

ENST00000695997.1:n.433+805dup

ENST00000696003.1:n.488dup

ENST00000696004.1:n.488dup

ENST00000696006.1:c.396dup

ENST00000696007.1:c.329+805dup

ENST00000696008.1:n.312dup

ENST00000696009.1:n.507dup

ENST00000696017.1:c.393dup

ENST00000696034.1:c.396dup

ENST00000696035.1:n.506dup

ENST00000696036.1:n.1086dup

ENST00000696037.1:n.2073dup

	ENST00000696038.1:c.*142dup ENST00000696039.1:n.684dup ENST00000696058.1:c.396dup ENST00000696059.1:c.*341dup ENST00000696060.1:c.396dup ENST00000696061.1:c.393dup ENST00000696062.1:c.459dup ENST00000696063.1:c.471dup ENST00000696064.1:c.243dup ENST00000696065.1:c.66-2721dup ENST00000696075.1:c.*366dup ENST00000696076.1:c.396dup ENST00000696077.1:c.393dup ENST00000696078.1:c.396dup ENST00000696079.1:c.396dup ENST00000696080.1:c.396dup ENST00000696082.1:c.474dup ENST00000696083.1:n.38dup ENST00000696084.1:n.497dup ENST00000696104.1:c.362+805dup ENST00000696105.1:c.396dup ENST00000372874.9:c.396dup ENST00000372874.8:c.396dup ENST00000464097.5:n.70dup ENST00000492931.5:n.480dup ENST00000536532.5:c.396dup ENST00000537820.1:c.396dup ENST00000539235.5:c.219-2573dup NM_000022.2:c.396dup NM_000022.3:c.396dup NM_001322050.1:c.73+805dup NM_001322051.1:c.396dup NR_136160.1:n.547dup NM_001322050.2:c.73+805dup NM_001322051.2:c.396dup NR_136160.2:n.488dup
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Pathogenic

Met criteria codes 3

PVS1 PP4 PM2_Supporting

Not Met criteria codes 1

PM3

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 c.396dup (p.Val133Serfs*38) (NM_000022.4) variant in ADA is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 5/12 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). At least one patient with this variant displayed Diagnostic criteria for Leaky SCID (0.5pt) + T-B-NK- lymphocyte subset profile (0.5pt) = 1 point TOTAL, which is highly specific for SCID (PP4_Met, PMID: 21664875). 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: PVS1, PM2_Supporting, and PP4. (VCEP specifications version 1).

Met criteria codes

PVS1			The c.396dup (p.Val133Serfs*38) (NM_000022.4) variant in ADA is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 5/12 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4			At least one patient with this variant displayed Diagnostic criteria for Leaky SCID (0.5pt) + T-B-NK- lymphocyte subset profile (0.5pt) = 1 point TOTAL, which is highly specific for SCID (PP4_Met, PMID: 21664875).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Not Met criteria codes

PM3			PMID 21664875, patient #69: The patient was diagnosed with atypical SCID. The patient was compound heterozygous with another variant not yet curated by the SCID VCEP (c.780+1G>A: This variant will not be evaluated now because the pathogenic level was already reached.)
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Curation History



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