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Variant: NM_000022.4(ADA):c.603C>A (p.Tyr201Ter)

Version: 1.0

CA409120739

1406981 (ClinVar)

Gene: ADA (HGNC:100)
Condition: adenosine deaminase deficiency (MONDO:0007064)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7d1b7701-e63b-4ddc-a6e4-5d2a6e0c932a
Approved on: 2024/4/4
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HGVS expressions

NM_000022.4:c.603C>A
NM_000022.4(ADA):c.603C>A (p.Tyr201Ter)
NC_000020.11:g.44624205G>T
CM000682.2:g.44624205G>T
NC_000020.10:g.43252846G>T
CM000682.1:g.43252846G>T
NC_000020.9:g.42686260G>T
NG_007385.1:g.32531C>A
ENST00000492931.6:n.694C>A
ENST00000536076.2:c.450C>A
ENST00000536532.6:c.603C>A
ENST00000537820.2:c.603C>A
ENST00000539235.6:c.219-1127C>A
ENST00000695889.1:c.219-1275C>A
ENST00000695890.1:n.2406C>A
ENST00000695891.1:c.219-1275C>A
ENST00000695927.1:c.681C>A
ENST00000695949.1:c.600C>A
ENST00000695957.1:c.*94C>A
ENST00000695991.1:c.217-1275C>A
ENST00000695992.1:c.603C>A
ENST00000695993.1:c.603C>A
ENST00000695994.1:c.603C>A
ENST00000695995.1:c.217-1127C>A
ENST00000695996.1:n.674C>A
ENST00000695997.1:n.558C>A
ENST00000696003.1:n.695C>A
ENST00000696004.1:n.695C>A
ENST00000696005.1:c.125C>A
ENST00000696006.1:c.603C>A
ENST00000696007.1:c.454C>A
ENST00000696008.1:n.1758C>A
ENST00000696009.1:n.1953C>A
ENST00000696017.1:c.600C>A
ENST00000696034.1:c.603C>A
ENST00000696035.1:n.713C>A
ENST00000696036.1:n.1293C>A

ENST00000696037.1:n.2280C>A
ENST00000696038.1:c.*349C>A
ENST00000696039.1:n.891C>A
ENST00000696058.1:c.603C>A
ENST00000696059.1:c.*548C>A
ENST00000696060.1:c.603C>A
ENST00000696061.1:c.600C>A
ENST00000696062.1:c.666C>A
ENST00000696063.1:c.678C>A
ENST00000696064.1:c.450C>A
ENST00000696065.1:c.66-1275C>A
ENST00000696074.1:n.219C>A
ENST00000696075.1:c.*573C>A
ENST00000696076.1:c.603C>A
ENST00000696077.1:c.600C>A
ENST00000696078.1:c.603C>A
ENST00000696079.1:c.603C>A
ENST00000696080.1:c.603C>A
ENST00000696081.1:n.722C>A
ENST00000696082.1:c.681C>A
ENST00000696083.1:n.1484C>A
ENST00000696084.1:n.704C>A
ENST00000696104.1:c.363-1275C>A
ENST00000696105.1:c.*144C>A
ENST00000372874.9:c.603C>A
ENST00000372874.8:c.603C>A
ENST00000372887.5:c.*229G>T
ENST00000464097.5:n.277C>A
ENST00000492931.5:n.687C>A
ENST00000536532.5:c.603C>A
ENST00000537820.1:c.603C>A
ENST00000539235.5:c.219-1127C>A
NM_000022.2:c.603C>A
NM_000022.3:c.603C>A
NM_001322050.1:c.198C>A
NM_001322051.1:c.603C>A
NR_136160.1:n.754C>A
NM_001322050.2:c.198C>A
NM_001322051.2:c.603C>A
NR_136160.2:n.695C>A

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

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

The c.603C>A (p.Tyr201Ter) (NM_000022.4) variant in ADA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 6/12 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1_Met). The highest population minor allele frequency in gnomAD v4 is 0.00001166 (1/85734 alleles) in South Asian population, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). There are no publications for this variant in the literature. As per the SCID VCEP specifications and the Bayesian interpretation of the ACMG/AMP combining rules, 1 very strong and 1 supporting criteria results in a Likely Pathogenic classification. In summary, this variant meets the criteria to be classified as 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: PM2_supporting,PVS1 (VCEP specifications version 1).

Met criteria codes

PVS1	✔	The c.603C>A (p.Tyr201Ter) (NM_000022.4) variant in ADA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 6/12 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1 Met).
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4 is 0.00001166 (1/85734 alleles) in South Asian population, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

Curation History

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