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

Version: 1.0

CA409120740

555182 (ClinVar)

Gene: ADA (HGNC:100)
Condition: adenosine deaminase deficiency (MONDO:0007064)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3d3dd172-f31e-4e3e-b101-075568b4d23a
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HGVS expressions

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

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

Pathogenic

Met criteria codes 3

PM2_Supporting PM3 PVS1

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>G (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 0.00002992 (1/33422 alleles) in African/African American 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. Patient # 46 was found to be heterozygous for c.603C>G (p.Tyr201*) and c.632G>A (p.Arg211His) which is classified as pathogenic for SCID by the ClinGen SCID VCEP (1 pt.) (PMID: 26255240, PM3). In summary, this variant meets the criteria to be classified as a 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,PM3,PVS1 (VCEP specifications version 1).

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4 is 0.00002992 (1/33422 alleles) in African/African American 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.
PM3	✔	Patient # 46 was found to be heterozygous for c.603C>G (p.Tyr201*) and c.632G>A (p.Arg211His) which is classified as pathogenic for SCID by the ClinGen SCID VCEP (1 pt.) (PMID: 26255240, PM3)
PVS1	✔	The c.603C>G (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).

Curation History

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