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Variant: NM_000022.4(ADA):c.516C>A (p.Tyr172Ter)

Version: 1.0

CA9871639

983781 (ClinVar)

Gene: ADA (HGNC:100)
Condition: adenosine deaminase deficiency (MONDO:0007064)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4edc6d6a-2dfd-4677-b7ef-90727f737d51
Approved on: 2024/5/28
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HGVS expressions

NM_000022.4(ADA):c.516C>A (p.Tyr172Ter)
NM_000022.4:c.516C>A
NC_000020.11:g.44624292G>T
CM000682.2:g.44624292G>T
NC_000020.10:g.43252933G>T
CM000682.1:g.43252933G>T
NC_000020.9:g.42686347G>T
NG_007385.1:g.32444C>A
ENST00000492931.6:n.607C>A
ENST00000536076.2:c.363C>A
ENST00000536532.6:c.516C>A
ENST00000537820.2:c.516C>A
ENST00000539235.6:c.219-1214C>A
ENST00000695889.1:c.219-1362C>A
ENST00000695890.1:n.2319C>A
ENST00000695891.1:c.219-1362C>A
ENST00000695927.1:c.594C>A
ENST00000695949.1:c.513C>A
ENST00000695957.1:c.*7C>A
ENST00000695991.1:c.217-1362C>A
ENST00000695992.1:c.516C>A
ENST00000695993.1:c.516C>A
ENST00000695994.1:c.516C>A
ENST00000695995.1:c.217-1214C>A
ENST00000695996.1:n.587C>A
ENST00000695997.1:n.471C>A
ENST00000696003.1:n.608C>A
ENST00000696004.1:n.608C>A
ENST00000696005.1:c.38C>A
ENST00000696006.1:c.516C>A
ENST00000696007.1:c.367C>A
ENST00000696008.1:n.1671C>A
ENST00000696009.1:n.1866C>A
ENST00000696017.1:c.513C>A
ENST00000696034.1:c.516C>A
ENST00000696035.1:n.626C>A
ENST00000696036.1:n.1206C>A

ENST00000696037.1:n.2193C>A
ENST00000696038.1:c.*262C>A
ENST00000696039.1:n.804C>A
ENST00000696058.1:c.516C>A
ENST00000696059.1:c.*461C>A
ENST00000696060.1:c.516C>A
ENST00000696061.1:c.513C>A
ENST00000696062.1:c.579C>A
ENST00000696063.1:c.591C>A
ENST00000696064.1:c.363C>A
ENST00000696065.1:c.66-1362C>A
ENST00000696074.1:n.132C>A
ENST00000696075.1:c.*486C>A
ENST00000696076.1:c.516C>A
ENST00000696077.1:c.513C>A
ENST00000696078.1:c.516C>A
ENST00000696079.1:c.516C>A
ENST00000696080.1:c.516C>A
ENST00000696081.1:n.635C>A
ENST00000696082.1:c.594C>A
ENST00000696083.1:n.1397C>A
ENST00000696084.1:n.617C>A
ENST00000696104.1:c.363-1362C>A
ENST00000696105.1:c.*57C>A
ENST00000372874.9:c.516C>A
ENST00000372874.8:c.516C>A
ENST00000464097.5:n.190C>A
ENST00000492931.5:n.600C>A
ENST00000536532.5:c.516C>A
ENST00000537820.1:c.516C>A
ENST00000539235.5:c.219-1214C>A
NM_000022.2:c.516C>A
NM_000022.3:c.516C>A
NM_001322050.1:c.111C>A
NM_001322051.1:c.516C>A
NR_136160.1:n.667C>A
NM_001322050.2:c.111C>A
NM_001322051.2:c.516C>A
NR_136160.2:n.608C>A

Likely Pathogenic

Met criteria codes 2

PM2_Supporting 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.516C>A (p.Tyr172Ter) (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 filtering allele frequency (the upper threshold of the 95% CI of 5/86250) of the c.516C>A variant in ADA is 0.00002194 for South Asian chromosomes by gnomAD v4, 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 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: PVS1, PM2_supporting.

Met criteria codes

PM2_Supporting	✔	The filtering allele frequency (the upper threshold of the 95% CI of 5/86250) of the c.516C>A variant in ADA is 0.00002194 for South Asian chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.0001742) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).
PVS1	✔	The c.516C>A (p.Tyr172Ter) (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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