

Variant: *NM_005214.5(CTLA4):c.516G>A (p.Ser172=)*

Version: 1.0

CA2067126 [↗](#)

1143236 (ClinVar) [↗](#)

Gene: CTLA4 ([HGNC:1493](#))

Condition: autoimmune lymphoproliferative syndrome due to CTLA4 haploinsufficiency ([MONDO:0014493](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 31bec57e-3750-4d8f-9ea4-59ac5cd38d92

Approved on: 2025/11/24

Published on: 2025/12/2

HGVS expressions

NM_005214.5:c.516G>A

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NC_000002.12:g.203871436G>A

CM000664.2:g.203871436G>A

NC_000002.11:g.204736159G>A

CM000664.1:g.204736159G>A

NC_000002.10:g.204444404G>A

NG_011502.1:g.8651G>A

ENST00000696049.1:c.507+9G>A

ENST00000696479.1:c.588G>A

ENST00000427473.3:n.491+503G>A

ENST00000648405.2:c.516G>A

ENST00000650075.1:n.540G>A

ENST00000295854.10:c.457+503G>A

ENST00000302823.7:c.516G>A

ENST00000427473.2:c.346+503G>A

ENST00000472206.1:c.172+788G>A

ENST00000487393.1:n.110-1272G>A

NM_001037631.2:c.457+503G>A

NM_005214.4:c.516G>A

NM_001037631.3:c.457+503G>A

Benign

Met criteria codes **1**

BA1

Not Met criteria codes **2**

BP4

BP7

Evidence Links **0**

Expert Panel

Antibody Deficiencies VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Antibody Deficiencies Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CTLA4 Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Antibody Deficiencies VCEP

NM_005214.5(CTLA4):c.516G>A (p.Ser172=) is a synonymous variant in exon 2 but has an intermediate prediction of impact at splicing sites, so BP7 is not met. The splicing impact predictor SpliceAI gives a delta score of 0.10 for donor loss, which is higher than the ClinGen Antibody Deficiencies VCEP recommended threshold of <0.1 and does not meet the BP4 code. This variant is present in gnomAD v4.1.0 at a GrpMax allele frequency of 0.0005198, with 50 alleles / 74,906 total alleles in the African / African-American population, which is higher than the ClinGen Antibody Deficiencies VCEP BA1 threshold of >0.0000111 (BA1). In summary, this variant meets the criteria to be classified as benign for autosomal dominant autoimmune lymphoproliferative syndrome due to CTLA4 haploinsufficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Antibody Deficiencies VCEP: BA1. (VCEP specifications version 1.0.0; date of approval 09/18/2025).

Met criteria codes

BA1			This variant is present in gnomAD v4.1.0 at a GrpMax allele frequency of 0.0005198, with 50 alleles / 74,906 total alleles in the African / African-American population, which is higher than the ClinGen Antibody Deficiencies VCEP BA1 threshold of >0.0000111 (BA1).
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Not Met criteria codes

BP4			The splicing impact predictor SpliceAI gives a delta score of 0.10 for donor loss, which is higher than the ClinGen Antibody Deficiencies VCEP recommended threshold of <0.1 and does not meet the BP4 code.
BP7			The synonymous variant NM_005214.5(CTLA4):c.516G>A (p.Ser172=) has an intermediate prediction of impact at splicing sites according to Splice AI, so BP7 is not met.

Curation History



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