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Variant: NM_005026.5(PIK3CD):c.1777G>C (p.Gly593Arg)

Version: 1.0

CA577321

424409 (ClinVar)

Gene: PIK3CD (HGNC:5293)
Condition: immunodeficiency 14 (MONDO:0014222)
Inheritance Mode: Autosomal dominant inheritance
UUID: 34a7a3b6-fbec-4062-99dd-2ea897cd9d99
Approved on: 2025-12-19
Published on: 2025-12-23

HGVS expressions

NM_005026.5:c.1777G>C
NM_005026.5(PIK3CD):c.1777G>C (p.Gly593Arg)
NC_000001.11:g.9721214G>C
CM000663.2:g.9721214G>C
NC_000001.10:g.9781272G>C
CM000663.1:g.9781272G>C
NC_000001.9:g.9703859G>C
NG_023434.1:g.74483G>C
ENST00000481137.2:c.*1031G>C
ENST00000698709.1:c.1777G>C
ENST00000698710.1:c.1774G>C
ENST00000698712.1:c.1777G>C
ENST00000698713.1:c.1777G>C
ENST00000698714.1:c.1777G>C
ENST00000698715.1:c.1774G>C
ENST00000698716.1:c.1765G>C
ENST00000698718.1:n.847G>C
ENST00000698719.1:n.79G>C
ENST00000698789.1:c.453G>C
ENST00000377346.9:c.1777G>C
ENST00000361110.6:c.1849G>C
ENST00000377346.8:c.1777G>C
ENST00000536656.5:c.1849G>C
ENST00000543390.2:c.1849G>C
ENST00000628140.2:c.1849G>C
NM_005026.3:c.1777G>C
NM_001350234.1:c.1774G>C
NM_001350235.1:c.1690G>C
NM_005026.4:c.1777G>C
NM_001350234.2:c.1774G>C

Likely Benign

Met criteria codes 1

BP4

Not Met criteria codes 3

PS4 PP4 BS1

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 PIK3CD Version 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Antibody Deficiencies VCEP

NM_005026.5(PIK3CD):c.1777G>C (p.Gly593Arg) is a missense variant causing substitution of glycine by arginine at amino acid 593. This variant is present in gnomAD v4.1.0 at a total combined allele frequency of 0.0002405, with 388 alleles / 1,613,342 total alleles across all populations of gnomAD, which is higher than the ClinGen Antibody Deficiencies VCEP PM2_Supporting threshold of <0.00000132. The variant is present in gnomAD v.4.1.0 at a GrpMax allele frequency of 0.0002731, with 353 alleles / 1,180,006 total alleles in the European (non-Finnish) population, which is lower than the BS1 threshold of >0.000316, so no population code can be applied. This variant has been reported in a ClinVar submission of a proband with a phenotype including recurrent pneumonia (4 pts), asthma and cough with eosinophilic infiltration of the esophagus (0.5 pts), and anxiety, with the peripheral blood indicating that transitional B cells and T follicular helper cells were both within the normal ranges, while activated blasting primary T cells showed no increase in phospho-AKT upon anti-CD3 stimulation compared to controls, and no increased baseline pS6 (SCV005423652.1). Together, these are not sufficiently specific for immunodeficiency 14 for inclusion in PS4_Supporting. The computational predictor REVEL gives a score of 0.144, which is below the ClinGen Antibody Deficiencies VCEP threshold of <0.290 and predicts a non-damaging effect on PIK3CD function. The computational predictor CADD gives a PHRED score of 19.41, which is below the ClinGen Antibody Deficiencies VCEP threshold of <22.7 and predicts a non-deleterious effect on PIK3CD function. The two predictors agree on a non-damaging effect (BP4). In summary, this variant meets the criteria to be classified as likely benign for autosomal dominant immunodeficiency 14 based on the ACMG/AMP criteria applied, as specified by the ClinGen Antibody Deficiencies VCEP: BP4. (VCEP specifications version 1.0.0).

Met criteria codes

BP4	✔	The computational predictor REVEL gives a score of 0.144, which is below the ClinGen Antibody Deficiencies VCEP threshold of <0.290 and predicts a non-damaging effect on PIK3CD function. The computational predictor CADD gives a PHRED score of 19.41, which is below the ClinGen Antibody Deficiencies VCEP threshold of <22.7 and predicts a non-deleterious effect on PIK3CD function. The two predictors agree on a non-damaging effect (BP4).

Not Met criteria codes

PS4	✖	This variant has been reported in a ClinVar submission of a proband with a phenotype including recurrent pneumonia (4 pts), asthma and cough with eosinophilic infiltration of the esophagus (0.5 pts), and anxiety, with the peripheral blood indicating that transitional B cells and T follicular helper cells were both within the normal ranges, while activated blasting primary T cells showed no increase in phospho-AKT upon anti-CD3 stimulation compared to controls, and no increased baseline pS6 (SCV005423652.1). Together, these are not sufficiently specific for immunodeficiency 14 for inclusion in PS4_Supporting.
PP4	✖	

This variant has been reported in a ClinVar submission of a proband with a phenotype including recurrent pneumonia (4 pts), asthma and cough with eosinophilic infiltration of the esophagus (0.5 pts), and anxiety, with the peripheral blood indicating that transitional B cells and T follicular helper cells were both within the normal ranges, while activated blasting primary T cells showed no increase in phospho-AKT upon anti-CD3 stimulation compared to controls, and no increased baseline pS6 (SCV005423652.1). Together, these are not sufficiently specific for immunodeficiency 14 to meet PP4.

BS1 ✖ This variant is present in gnomAD v.4.1.0 at a GrpMax allele frequency of 0.0002731, with 353 alleles / 1,180,006 total alleles in the European (non-Finnish) population, which is lower than the BS1 threshold of >0.000316, so no population code can be applied.

Curation History

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