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Variant: NM_000206.3(IL2RG):c.1061A>G (p.His354Arg)

Version: 2.0

CA10443761

1199323 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: c507f13c-43cd-4cfe-b95f-fa1e3960702c
Approved on: 2024/1/26
Published on: 2024/1/26

HGVS expressions

NM_000206.3(IL2RG):c.1061A>G (p.His354Arg)
NM_000206.3:c.1061A>G
NC_000023.11:g.71107785T>C
CM000685.2:g.71107785T>C
NC_000023.10:g.70327635T>C
CM000685.1:g.70327635T>C
NC_000023.9:g.70244360T>C
NG_009088.1:g.8769A>G
NG_021141.1:g.4004A>G
ENST00000482750.6:c.*181A>G
ENST00000696903.1:n.1364A>G
ENST00000374202.7:c.1061A>G
ENST00000642473.1:n.1288+492A>G
ENST00000644022.1:n.1190+492A>G
ENST00000644708.1:n.1302+68A>G
ENST00000644911.1:n.1399+68A>G
ENST00000645266.1:c.924+492A>G
ENST00000645518.1:c.924+492A>G
ENST00000646106.1:c.993+68A>G
ENST00000646505.1:c.924+492A>G
ENST00000647492.1:c.924+492A>G
ENST00000276110.6:n.1654A>G
ENST00000374188.7:c.248A>G
ENST00000374202.6:c.1061A>G
ENST00000456850.6:c.491A>G
ENST00000482750.5:c.377A>G
ENST00000512747.3:n.1595A>G
NM_000206.2:c.1061A>G

Likely Benign

Met criteria codes 1
BS2

Not Met criteria codes 1
PM2

Expert Panel
Severe Combined Immunodeficiency Disease VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for IL2RG Version 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000206.3(IL2RG):c.1061A>G is a missense variant predicted to cause substitution of Histidine by Arginine at amino acid 354 (p.His354Arg). The filtering allele frequency (the upper threshold of the 95% CI of 7/30447) of the c.1061A>G variant in IL2RG is 0.0001216 for East Asian chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000124) for PM2_Supporting. However, 4 hemizygotes were reported (PM2 not met).The variant is observed in 4 hemizygotes in gnomAD v4 (BS2_Strong). To our knowledge, this variant has not been reported in the literature in individuals affected with IL2RG related conditions or in functional studies. In summary, this variant meets the criteria to be classified as likely benign variant for X-linked severe combined immunodeficiency due to IL2RG deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: BS2 (VCEP specifications version 1).

Met criteria codes

BS2	✔	The variant is observed in 4 hemizygotes in gnomAD v4 (BS2_Strong).

Not Met criteria codes

PM2	✖	The filtering allele frequency (the upper threshold of the 95% CI of 7/30447) of the c.1061A>G variant in IL2RG is 0.0001216 for East Asian chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000124) for PM2_Supporting. However, 4 hemizygotes were reported (PM2 not met).

Curation History

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