The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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

*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**: 2024-01-26
**Published on**: 2024-01-26

## *HGVS expressions*

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

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 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

| See Report | Preferred Variant Title | Classification | Condition | Published Date | Version | Criteria Specification | Gene |
|---|---|---|---|---|---|---|---|

No matching records found