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.455T>G (p.Val152Gly)*

Version: 1.0

*CA413496508*

*624584 (ClinVar)*

**Gene**: IL2RG (HGNC:3561)
**Condition**: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
**Inheritance Mode**: X-linked inheritance
**UUID:** 6b44a96e-4725-4e0f-adb2-46375b66f326
**Approved on**: 2026/2/20
**Published on**: 2026/4/24

## *HGVS expressions*

**NM_000206.3:c.455T>G**
**NM_000206.3(IL2RG):c.455T>G (p.Val152Gly)**
NC_000023.11:g.71110295A>C
CM000685.2:g.71110295A>C
NC_000023.10:g.70330145A>C
CM000685.1:g.70330145A>C
NC_000023.9:g.70246870A>C
NG_009088.1:g.6259T>G
NG_021141.1:g.1494T>G
ENST00000482750.6:c.455T>G
ENST00000696903.1:n.506T>G
ENST00000374202.7:c.455T>G
ENST00000642473.1:n.819T>G
ENST00000644022.1:n.860+209T>G
ENST00000644708.1:n.861T>G
ENST00000644911.1:n.861T>G
ENST00000645266.1:c.455T>G
ENST00000645518.1:c.455T>G
ENST00000646106.1:c.455T>G
ENST00000646505.1:c.455T>G
ENST00000647492.1:c.455T>G
ENST00000276110.6:n.1048T>G
ENST00000374188.7:c.-262T>G
ENST00000374202.6:c.455T>G
ENST00000456850.6:c.25-905T>G
ENST00000464642.5:c.323T>G
ENST00000487883.1:c.419T>G
ENST00000512747.3:n.521+209T>G
NM_000206.2:c.455T>G

**Likely Pathogenic**

**Met criteria codes** 4

PM5 PS4_Supporting PP4_Strong PM2_Supporting

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 2.1.0*

**Criteria Specification Approval History**

**Criteria Specifications for this VCEP**

## Evidence submitted by expert panel

***Severe Combined Immunodeficiency Disease VCEP***

**The NM_000206.3:c.455T>G variant in IL2RG is a missense variant predicted to cause substitution of valine by glycine at amino acid 152 (p.Val152Gly). The variant is absent from gnomAD v4.1.0 (PM2_Supporting). The variant has been reported in two patients meeting the PP4 phenotypic criteria (PMIDs 31031743, 36177038) (PS4_Supporting). One patient was diagnosed with SCID (PMID 36177038). The patient showed a T-B+NK- lymphocyte profile and an absence of STAT5 phosphorylation upon IL-2 stimulation (other possible variants were not excluded). The lymphopenia was resolved by IL2RG gene therapy (CNV testing not reported) (PP4_Strong). Another missense variant c.455T>C (p.Val152Ala) in the same codon has been classified as pathogenic for SCID by the ClinGen SCID VCEP (PM5). In summary, this variant is classified as likely pathogenic for SCID. ACMG/AMP criteria applied, as specified by the ClinGen SCID-VCEP: PP4_Strong, PM2_Supporting, PM5, PS4_Supporting (VCEP specifications version 2.1).**

### Met criteria codes

| | | |
|---|---|---|
| **PM5** | ✔ | Another missense variant c.455T>C (p.Val152Ala), ClinVar Variation ID 36386, in the same codon has been classified as pathogenic for SCID by the ClinGen SCID VCEP. PM5 is met. |
| **PS4_Supporting** | ✔ | This variant has been reported in 2 patients meeting the PP4 phenotypic criteria (PMIDs 31031743, 36177038). Excluding the proband used to satisfy the PP4 criteria (PMID 36177038), the other patient is counted for PS4. PS4_Supporting is met. |
| **PP4_Strong** | ✔ | One individual with this variant was diagnosed with X-SCID (0.5pt) (PMID 36177038). The patient showed a T-B+NK- lymphocyte profile (0.5pt + 1pt), and an absence of STAT5 phosphorylation upon IL-2 stimulation (other possible variants were not excluded) (1.5pt). The lymphopenia was resolved by IL2RG gene therapy (CNV testing not reported, 4.5pt). 8pt in total, PP4_Strong is met. |
| **PM2_Supporting** | ✔ | This variant is absent from gnomAD v4.1.0. (PM2_Supporting) |

## Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.