Variant: NM_000206.3(IL2RG):c.455T>C (p.Val152Ala)

Version: 1.0

CA260413

36386 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: 55f9c9b6-4dae-488e-85e3-100295ce694f
Approved on: 2025-11-18
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HGVS expressions

NM_000206.3:c.455T>C
NM_000206.3(IL2RG):c.455T>C (p.Val152Ala)
NC_000023.11:g.71110295A>G
CM000685.2:g.71110295A>G
NC_000023.10:g.70330145A>G
CM000685.1:g.70330145A>G
NC_000023.9:g.70246870A>G
NG_009088.1:g.6259T>C
NG_021141.1:g.1494T>C
ENST00000482750.6:c.455T>C
ENST00000696903.1:n.506T>C
ENST00000374202.7:c.455T>C
ENST00000642473.1:n.819T>C
ENST00000644022.1:n.860+209T>C
ENST00000644708.1:n.861T>C
ENST00000644911.1:n.861T>C
ENST00000645266.1:c.455T>C
ENST00000645518.1:c.455T>C
ENST00000646106.1:c.455T>C
ENST00000646505.1:c.455T>C
ENST00000647492.1:c.455T>C
ENST00000276110.6:n.1048T>C
ENST00000374188.7:c.-262T>C
ENST00000374202.6:c.455T>C
ENST00000456850.6:c.25-905T>C
ENST00000464642.5:c.323T>C
ENST00000487883.1:c.419T>C
ENST00000512747.3:n.521+209T>C
NM_000206.2:c.455T>C

Pathogenic

Met criteria codes 3

PS4 PM2_Supporting PP4_Strong

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>C variant in IL2RG is a missense variant predicted to cause substitution of valine by alanine at amino acid 152 (p.Val152Ala). The variant is absent from gnomAD v4.1.0 (PM2_Supporting). The variant has been reported in five patients from four families meeting the PP4 phenotypic criteria (PMIDs 33628209, 8557662, 11129345, 25326637) (PS4_Strong). One male patient with this variant presented with SCID within a year of life (PMID 11129345). The patient showed a T-B+NK- lymphocyte profile, with T cell 18/mm3 (normal range 1700-3600/mm3); B cell 1120/mm3 (normal range 500-1500/mm3) and NK cell 31/mm3 (normal range 300-700/mm3). A flow cytometry assay showed that surface expression of CD132 was absent on patient blood cells (PP4_Strong). In summary, this variant meets the criteria to be classified as pathogenic for SCID. ACMG/AMP criteria applied, as specified by the ClinGen SCID-VCEP: PP4_Strong, PM2_Supporting, PS4_Strong (VCEP specifications version 2.1).

Met criteria codes

PS4	✔	This variant has been reported in 5 patients in 4 families meeting the PP4 phenotypic criteria (PMIDs 33628209, 8557662, 11129345, 25326637). Excluding the patient used to satisfy the PP4 criteria (PMID 11129345), 3 unrelated patients are counted for PS4. PS4_Strong is met.
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0. (PM2_Supporting)
PP4_Strong	✔	One male patient with this variant presented with SCID within a year of life (0.5pt + 0.5pt) (PMID 11129345). The patient showed a T-B+NK- lymphocyte profile, with T cell 18/mm3 (normal range 1700-3600/mm3); B cell 1120/mm3 (normal range 500-1500/mm3) and NK cell 31/mm3 (normal range 300-700/mm3) (0.5 pt + 1 pt). A flow cytometry assay showed that surface expression of CD132 was absent on patient blood cells (4.5 pts). 7pt in total, PP4_Strong is met.

Curation History

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