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Variant: NM_000206.3(IL2RG):c.545G>A (p.Cys182Tyr)

Version: 1.3

CA16621484

419664 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: 1999996a-5910-405a-bb2e-51c3ec48dcce
Approved on: 2024/1/10
Published on: 2024/1/10

HGVS expressions

NM_000206.3:c.545G>A
NM_000206.3(IL2RG):c.545G>A (p.Cys182Tyr)
NC_000023.11:g.71110205C>T
CM000685.2:g.71110205C>T
NC_000023.10:g.70330055C>T
CM000685.1:g.70330055C>T
NC_000023.9:g.70246780C>T
NG_009088.1:g.6349G>A
NG_021141.1:g.1584G>A
ENST00000482750.6:c.545G>A
ENST00000696903.1:n.596G>A
ENST00000374202.7:c.545G>A
ENST00000642473.1:n.909G>A
ENST00000644022.1:n.860+299G>A
ENST00000644708.1:n.951G>A
ENST00000644911.1:n.951G>A
ENST00000645266.1:c.545G>A
ENST00000645518.1:c.545G>A
ENST00000646106.1:c.545G>A
ENST00000646505.1:c.545G>A
ENST00000647492.1:c.545G>A
ENST00000276110.6:n.1138G>A
ENST00000374188.7:c.-172G>A
ENST00000374202.6:c.545G>A
ENST00000456850.6:c.25-815G>A
ENST00000464642.5:c.413G>A
ENST00000487883.1:c.509G>A
ENST00000512747.3:n.521+299G>A
NM_000206.2:c.545G>A

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PP4_Moderate PS4

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.545G>A is a missense variant predicted to cause substitution of Cysteine by Tyrosine at amino acid 182 (p.Cys182Tyr). The variant is absent in gnomAD v4 (PM2_supporting). Male patient (0.5 pt.) with SCID (0.5 pt.), genome sequencing conducted (1 pt.),Reduced IL2-induced phosphorylation of STAT5 (1 pt.), T-B+NK- lymphocyte subset profile (0.5 pt.); total :3.5 pts (PP4_Moderate) PMID: 18688286. This variant has been reported in 6 probands (PS4_met, 5pts)(PMIDs: 25109802,22039266,18688286,35482138, 21865537,18728247) Another missense variant Cys182Arg in the same codon has been reported (PMID: 10794430) (not classified by SCID VCEP yet) (PM5 not evaluated). In summary, this variant meets the criteria to be classified as a Likely Pathogenic 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: PM2_supporting,PP4_Moderate, PS4_met(VCEP specifications version 1).

Met criteria codes

PM2_Supporting	✔	The variant is absent in gnomAD v4 (PM2_supporting).
PP4_Moderate	✔	Male patient (0.5 pt.) with SCID (0.5 pt.), genome sequencing conducted (1 pt.),Reduced IL2-induced phosphorylation of STAT5 (1 pt.), T-B+NK- lymphocyte subset profile (0.5 pt.); total :3.5 pts (PP4_Moderate) (PMID: 18688286).
PS4	✔	This variant has been reported in 6 probands (PS4_met, 5pts)(PMIDs: 25109802,22039266,18688286,35482138, 21865537,18728247)

Curation History

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