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Variant: NM_000206.3(IL2RG):c.184T>C (p.Cys62Arg)

Version: 1.0

CA413497163

1066149 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: a02c3b22-ff9e-46c7-8d9b-f6626fccdd0d
Approved on: 2024/6/12
Published on: 2024/6/12

HGVS expressions

NM_000206.3:c.184T>C
NM_000206.3(IL2RG):c.184T>C (p.Cys62Arg)
NC_000023.11:g.71110982A>G
CM000685.2:g.71110982A>G
NC_000023.10:g.70330832A>G
CM000685.1:g.70330832A>G
NC_000023.9:g.70247557A>G
NG_009088.1:g.5572T>C
NG_021141.1:g.807T>C
ENST00000482750.6:c.184T>C
ENST00000696903.1:n.235T>C
ENST00000374202.7:c.184T>C
ENST00000642473.1:n.548T>C
ENST00000644022.1:n.590T>C
ENST00000644708.1:n.590T>C
ENST00000644911.1:n.590T>C
ENST00000645266.1:c.184T>C
ENST00000645518.1:c.184T>C
ENST00000646106.1:c.184T>C
ENST00000646505.1:c.184T>C
ENST00000647492.1:c.184T>C
ENST00000276110.6:n.569T>C
ENST00000374188.7:c.-533T>C
ENST00000374202.6:c.184T>C
ENST00000456850.6:c.24+443T>C
ENST00000464642.5:c.52T>C
ENST00000473378.1:c.121T>C
ENST00000487883.1:c.148T>C
ENST00000512747.3:n.251T>C
NM_000206.2:c.184T>C

Pathogenic

Met criteria codes 5

PS4_Supporting | PM5 | PM1_Strong | PP4_Moderate | 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 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.184T>C is a missense variant predicted to cause substitution of Cysteine by Arginine at amino acid 62 (p.Cys62Arg). This mutation affects conserved cysteine residue i.e. Cys62 (PM1_strong). The variant is absent in gnomAD v4 (PM2_supporting). Male patient (0.5 pt.) with SCID (0.5 pt.), genome sequencing conducted (1 pt.),T-B+NK- lymphocyte subset profile (0.5 pt.); total : 2.5 pts (PP4_Moderate) (Invitae).Another missense variant [NM_000206.3(IL2RG):c.186T>A (p.Cys62Ter)] in the same codon has been reported (classified as pathogenic by SCID VCEP) (PM5 met).The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls (Invitae, PMID: 27484032) (PS4_supporting). In summary, this variant meets the criteria to be classified as a 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: PM1_strong, PM2_supporting, PP4_Moderate,PM5 met,PS4_supporting (VCEP specifications version 1).

Met criteria codes

PS4_Supporting	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls (Invitae, PMID: 27484032) (PS4_supporting).
PM5	✔	Another missense variant [NM_000206.3(IL2RG):c.186T>A (p.Cys62Ter)] in the same codon has been reported (classified as pathogenic by SCID VCEP) (PM5 met).
PM1_Strong	✔	This mutation affects conserved cysteine residue i.e. Cys62 (PM1_strong).
PP4_Moderate	✔	Male patient (0.5 pt.) with SCID (0.5 pt.), genome sequencing conducted (1 pt.),T-B+NK- lymphocyte subset profile (0.5 pt.); total : 2.5 pts (PP4_Moderate) (Invitae).
PM2_Supporting	✔	The variant is absent in gnomAD v4 (PM2_supporting).

Curation History

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