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Variant: NM_000206.3(IL2RG):c.738G>A (p.Trp246Ter)

Version: 1.0

CA413495835

1411137 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: 0b50e961-283c-403f-9d0f-e922f4740707
Approved on: 2024/6/13
Published on: 2024/6/13

HGVS expressions

NM_000206.3:c.738G>A
NM_000206.3(IL2RG):c.738G>A (p.Trp246Ter)
NC_000023.11:g.71109247C>T
CM000685.2:g.71109247C>T
NC_000023.10:g.70329097C>T
CM000685.1:g.70329097C>T
NC_000023.9:g.70245822C>T
NG_009088.1:g.7307G>A
NG_021141.1:g.2542G>A
ENST00000482750.6:c.738G>A
ENST00000696903.1:n.789G>A
ENST00000374202.7:c.738G>A
ENST00000642473.1:n.1102G>A
ENST00000644022.1:n.1004G>A
ENST00000644708.1:n.1144G>A
ENST00000644911.1:n.1144G>A
ENST00000645266.1:c.738G>A
ENST00000645518.1:c.738G>A
ENST00000646106.1:c.738G>A
ENST00000646505.1:c.738G>A
ENST00000647492.1:c.738G>A
ENST00000276110.6:n.1331G>A
ENST00000374188.7:c.22G>A
ENST00000374202.6:c.738G>A
ENST00000456850.6:c.168G>A
ENST00000464642.5:c.606G>A
ENST00000482750.5:c.151G>A
ENST00000512747.3:n.665G>A
NM_000206.2:c.738G>A

Pathogenic

Met criteria codes 3

PM2_Supporting PP4 PVS1

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

The c.738G>A (p.Trp246Ter) variant in IL2RG is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 5/8, leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1 Met). This variant is absent from gnomAD v4 (PM2_Supporting). At least one proband in the literature presents: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5 pts) + XY male sex (0.5 pts), total is 1 point, PP4 is met. In summary, this variant meets the criteria to be classified as Pathogenic for X-linked T-B+ severe combined immunodeficiency due to gamma chain deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PVS1, PM2_Supporting, and PP4 (VCEP specifications version 1).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4 (PM2_Supporting).
PP4	✔	At least one proband in the literature presents: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5 pts) + XY male sex (0.5 pts), total is 1 point, PP4 is met.
PVS1	✔	The c.738G>A (p.Trp246Ter) variant in IL2RG is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 5/8, leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1 Met).

Curation History

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