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Variant: NM_000206.3(IL2RG):c.964C>T (p.Gln322Ter)

Version: 1.0

CA413628043

2138599 (ClinVar)

Gene: IL2RG (HGNC:3561)
Condition: T-B+ severe combined immunodeficiency due to gamma chain deficiency (MONDO:0010315)
Inheritance Mode: X-linked inheritance
UUID: c003ade5-11b1-4cf6-b78a-d11ecc369f9b
Approved on: 2024/6/13
Published on: 2024/6/13

HGVS expressions

NM_000206.3:c.964C>T
NM_000206.3(IL2RG):c.964C>T (p.Gln322Ter)
NC_000023.11:g.71107882G>A
CM000685.2:g.71107882G>A
NC_000023.10:g.70327732G>A
CM000685.1:g.70327732G>A
NC_000023.9:g.70244457G>A
NG_009088.1:g.8672C>T
NG_021141.1:g.3907C>T
ENST00000482750.6:c.*84C>T
ENST00000696903.1:n.1267C>T
ENST00000374202.7:c.964C>T
ENST00000642473.1:n.1288+395C>T
ENST00000644022.1:n.1190+395C>T
ENST00000644708.1:n.1273C>T
ENST00000644911.1:n.1370C>T
ENST00000645266.1:c.924+395C>T
ENST00000645518.1:c.924+395C>T
ENST00000646106.1:c.964C>T
ENST00000646505.1:c.924+395C>T
ENST00000647492.1:c.924+395C>T
ENST00000276110.6:n.1557C>T
ENST00000374188.7:c.151C>T
ENST00000374202.6:c.964C>T
ENST00000456850.6:c.394C>T
ENST00000482750.5:c.280C>T
ENST00000512747.3:n.1498C>T
NM_000206.2:c.964C>T

Pathogenic

Met criteria codes 3

PVS1 PP4 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

The c.964C>T (p.Gln322Ter) variant in IL2RG is a nonsense variant located in the last exon (8/8). Although it is not predicted to cause nonsense-mediated decay, as it is located in a critical region for protein function, PVS1 is still applied at default strength (PVS1). This variant is absent from gnomAD v4 (PM2_Supporting). At least one patient in the literature presents: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5 pts) + XY male sex (0.5 pts); The total is 1 point, PP4 is met (PMIDs: 33628209 and 9058718). 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

PVS1	✔	The c.964C>T (p.Gln322Ter) variant in IL2RG is a nonsense variant located in the last exon (8/8). Although it is not predicted to cause nonsense-mediated decay, as it is located in a critical region for protein function, PVS1 is still applied at default strength (PVS1).
PP4	✔	At least one patient in the literature presents: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5 pts) + XY male sex (0.5 pts); The total is 1 point, PP4 is met (PMIDs: 33628209 and 9058718).
PM2_Supporting	✔	This variant is absent from gnomAD v4 (PM2_Supporting).

Curation History

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