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Variant: NM_002185.5(IL7R):c.265C>T (p.Gln89Ter)

Version: 1.0

CA3231898

804345 (ClinVar)

Gene: IL7R (HGNC:3575)
Condition: severe combined immunodeficiency, autosomal recessive, T cell-negative, B cell-positive, NK cell-positive (MONDO:0012163)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5974917f-d7a0-4bc5-9ebd-d4f8705d0724
Approved on: 2024/1/17
Published on: 2024/1/17

HGVS expressions

NM_002185.5(IL7R):c.265C>T (p.Gln89Ter)
NM_002185.5:c.265C>T
NC_000005.10:g.35867349C>T
CM000667.2:g.35867349C>T
NC_000005.9:g.35867451C>T
CM000667.1:g.35867451C>T
NC_000005.8:g.35903208C>T
NG_009567.1:g.15461C>T
ENST00000303115.8:c.265C>T
ENST00000303115.7:c.265C>T
ENST00000506850.5:c.265C>T
ENST00000511031.1:n.399C>T
ENST00000511982.1:c.265C>T
ENST00000514217.5:c.265C>T
NM_002185.3:c.265C>T
NR_120485.1:n.368C>T
NM_002185.4:c.265C>T
NR_120485.2:n.394C>T
NR_120485.3:n.352C>T

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

BS2

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 IL7R Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The NM_002185.5(IL7R):c.265C>T (p.Gln89Ter) variant in IL7R is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 3/8, which is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The filtering allele frequency based on the European (non-Finnish) population (upper bound of 95% CI of 3/113430 alleles) is 0.000007030 in gnomAD v2.1.1, which is below the SCID-VCEP threshold (<0.00004129; PM2_Supporting). This variant has been reported in ClinVar and LOVD without patient information; however, it has not been reported in the literature to our knowledge. In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive SCID based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP. Criteria applied: PVS1, PM2_supporting (SCID VCEP specifications version 1.0).

Met criteria codes

PVS1	✔	The NM_002185.5(IL7R):c.265C>T (p.Gln89Ter) variant in IL7R is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 3/8, which is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	The filtering allele frequency based on the European (non-Finnish) population (upper bound of 95% CI of 3/113430 observed alleles) is 0.000007030 in gnomAD v2.1.1 which is below the SCID-VCEP threshold (<0.00004129) and therefore meets this criterion (PM2_Supporting).

Not Met criteria codes

BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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