The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000215.4(JAK3):c.175A>T (p.Lys59Ter)

Version: 1.0

CA404774961

1999662 (ClinVar)

Gene: JAK3 (HGNC:3718)
Condition: T-B+ severe combined immunodeficiency due to JAK3 deficiency (MONDO:0010938)
Inheritance Mode: Autosomal recessive inheritance
UUID: c9a1f1b7-afee-4d26-857e-d590482331f7
Approved on: 2024/1/17
Published on: 2024/1/17

HGVS expressions

NM_000215.4(JAK3):c.175A>T (p.Lys59Ter)
NM_000215.4:c.175A>T
NC_000019.10:g.17844243T>A
CM000681.2:g.17844243T>A
NC_000019.9:g.17955052T>A
CM000681.1:g.17955052T>A
NC_000019.8:g.17816052T>A
NG_007273.1:g.8749A>T
ENST00000526008.6:c.175A>T
ENST00000458235.7:c.175A>T
ENST00000458235.5:c.175A>T
ENST00000526008.5:n.275A>T
ENST00000527031.5:n.265A>T
ENST00000527670.5:c.175A>T
ENST00000528293.1:n.314A>T
ENST00000534444.1:c.175A>T
NM_000215.3:c.175A>T

Likely Pathogenic

Met criteria codes 2
PVS1 PM2_Supporting

Not Met criteria codes 4
PM5 BA1 BS1 PS1

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 JAK3 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_000215.4(JAK3):c.175A>T (p.Lys59Ter) variant in JAK3 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 2/24 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). To our knowledge, this variant has not been reported in the literature in individuals affected with JAK3-related conditions, and functional studies have not been found. 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 and PM2_supporting. (VCEP specifications version 1).

Met criteria codes

PVS1	✔	The NM_000215.4(JAK3):c.175A>T (p.Lys59Ter) variant in JAK3 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 2/24 leading to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Not Met criteria codes

PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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