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Variant: NM_000215.4(JAK3):c.307C>T (p.Arg103Cys)

Version: 1.0

CA9302208

384359 (ClinVar)

Gene: JAK3 (HGNC:3718)
Condition: T-B+ severe combined immunodeficiency due to JAK3 deficiency (MONDO:0010938)
Inheritance Mode: Autosomal recessive inheritance
UUID: c85a8c1d-d6af-48a6-a182-a644bdc1ba6c
Approved on: Thu, 01 Oct 2026 00:00:00 +0000
Published on: Tue, 27 Oct 2026 00:00:00 +0000

HGVS expressions

NM_000215.4:c.307C>T
NM_000215.4(JAK3):c.307C>T (p.Arg103Cys)
NC_000019.10:g.17843778G>A
CM000681.2:g.17843778G>A
NC_000019.9:g.17954587G>A
CM000681.1:g.17954587G>A
NC_000019.8:g.17815587G>A
NG_007273.1:g.9214C>T
ENST00000526008.6:c.307C>T
ENST00000458235.7:c.307C>T
ENST00000458235.5:c.307C>T
ENST00000526008.5:n.407C>T
ENST00000527031.5:n.397C>T
ENST00000527670.5:c.307C>T
ENST00000528293.1:n.324-287C>T
ENST00000534444.1:c.307C>T
NM_000215.3:c.307C>T

Likely Pathogenic

Met criteria codes 3

PM3_Strong | PM2_Supporting | PP4

Not Met criteria codes 11

PM1 | PM5 | PM4 | BA1 | BS1 | BS2 | BP4 | BP3 | BP1 | PP2 | PP3

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 2.3*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The c.307C>T (p.Arg103Cys) variant in JAK3 gene, that encodes for Janus kinase 3, has been reported in in compound heterozygous status with Cys227Profs*49 which is classified as pathogenic by the VCEP, in 1 patient with T-B+NK- SCID (PMID: 34173127) [1 pt]. This variant has also been reported along with R445* (Phase unknown) which is classified as pathogenic by the VCEP, in 1 patient [P073] with T-B+ SCID [0.5 pt]. NK cell data not available (PMID: 28747913). In addition, this variant is reported in compound heterozygous status with c.421-6C>T which is a VUS, in 1 patient [P55] with SCID (PMID: 30778343) [0.25pt]. Also reported in compound heterozygous status with p.Arg117His which is a VUS, in a Patient with T-B+NkLow SCID [0.25pt]. Total 2pts so PM3 met. This variant was found in a patient with T-B+NK- lymphocyte subset profile (PMID: 34173127) [0.5pt], in a patient whose diagnosis of Leaky/Atypical SCID was established (PMID: 30778343) [0.5pt] and in one patient whose Targeted gene panel testing was conducted using NGS and no alternative genetic explanation was found (PMID: 30778343) [1pt]. Total 1.5pts so PP4 met. The GrpMax filtering allele frequency of the European (Non-Finnish) population is 0.00000124 which is less than the threshold <0.000115 so PM2_supporting is met. Therefore, the c.307C>T (p.Arg103Cys) variant in JAK3 gene is classified as likely pathogenic, as per the ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for JAK3 Version 2.3. Evidence: PM3_Strong, PP4, PM2_Supporting

Met criteria codes

PM3_Strong	✔	Reported in compound heterozygous status with Cys227Profs*49 which is classified as pathogenic by the VCEP, in 1 patient with T-B+Nk- SCID (PMID: 34173127) [1 pt]. Reported along with R445* (Phase unknown) which is classified as pathogenic by the VCEP, in 1 patient [P073] with T-B+ SCID [0.5 pt]. NK cell data not available (PMID: 28747913). Reported in compound heterozygous status with c.421-6C>T which is a VUS, in 1 patient [P55] with SCID (PMID: 30778343) [0.25pt]. Reported in compound heterozygous status with p.Arg117His which is a VUS, in a Patient with T-B+NkLow SCID [0.25pt]. Total 2pts
PM2_Supporting	✔	The GrpMax filtering allele frequency of the European (Non-Finnish) population is 0.00000124 which is less than the threshold <0.000115 so PM2_supporting is met.
PP4	✔	This variant was found in a patient whose diagnosis of Leaky/Atypical SCID was established [0.5pt] and Targeted gene panel testing was conducted using NGS and no alternative genetic explanation was found (PMID: 30778343) [1pt]. Total 1.5pts

Not Met criteria codes

PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	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

BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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