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Variant: NM_000215.4(JAK3):c.1207C>T (p.Arg403Cys)

Version: 1.0

CA404770618

2138258 (ClinVar)

Gene: JAK3 (HGNC:3718)
Condition: T-B+ severe combined immunodeficiency due to JAK3 deficiency (MONDO:0010938)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1f594105-a7b2-4ae9-b79f-4dec3e1a01b2
Approved on: Mon, 28 Sep 2026 00:00:00 +0000
Published on: Tue, 27 Oct 2026 00:00:00 +0000

HGVS expressions

NM_000215.4(JAK3):c.1207C>T (p.Arg403Cys)
NM_000215.4:c.1207C>T
NC_000019.10:g.17840277G>A
CM000681.2:g.17840277G>A
NC_000019.9:g.17951086G>A
CM000681.1:g.17951086G>A
NC_000019.8:g.17812086G>A
NG_007273.1:g.12715C>T
ENST00000526008.6:c.1207C>T
ENST00000696967.1:n.384C>T
ENST00000458235.7:c.1207C>T
ENST00000458235.5:c.1207C>T
ENST00000526008.5:n.1307C>T
ENST00000527031.5:n.1297C>T
ENST00000527670.5:c.1207C>T
ENST00000528705.1:n.556C>T
ENST00000534444.1:c.1207C>T
NM_000215.3:c.1207C>T

Likely Pathogenic

Met criteria codes 3

PM5_Supporting PM3_Strong 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 JAK3 Version 2.3*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000215.4(JAK3):c.1207C>T is a missense variant predicted to cause substitution of Arginine by Cystine at amino acid 403 (p.Arg403Cys). The filtering allele frequency (the upper threshold of the 95% CI of 4/1461762) of the c.1352G>A variant in JAK3 is 2.999999999999999e-7 for Non-Finnish European chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000115) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). This variant has been reported in three affected individuals with SCID in the homozygous state (PMID: 26915675, 33040328, Invitae), two of whom were from consanguineous families (PM3 pts: 0.5+0.5+1 = 2). One affected individual was diagnosed by WES, with this JAK3 variant as the only reported candidate variant, and presented with a T−B+NK− lymphocyte subset profile (PMID: 33040328) (PP4 pts: 1+0.5=1.5). A different likely pathogenic missense variant affecting the same amino acid residue, c.1208G>A p.(Arg403His), has been observed in affected individuals with SCID (PMID: 31031743, ClinVar Variation ID: 803543). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for autosomal recessive severe combined immunodeficiency due to JAK3 deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PM3_Strong, PP4, PM5_Supporting, PM2_Supporting (VCEP specifications version 2.3).

Met criteria codes

PM5_Supporting	✔	A different likely pathogenic missense variant affecting the same amino acid residue, c.1208G>A p.(Arg403His), has been observed in affected individuals with SCID (PMID: 31031743, ClinVar Variation ID: 803543).
PM3_Strong	✔	This variant has been reported in three affected individuals with SCID in the homozygous state (PMID: 26915675, 33040328, Invitae), two of whom were from consanguineous families (PM3 pts: 0.5+0.5+1 = 2).
PM2_Supporting	✔	The filtering allele frequency (the upper threshold of the 95% CI of 4/1461762) of the c.1352G>A variant in JAK3 is 2.999999999999999e-7 for Non-Finnish European chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000115) for PM2_Supporting

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000215.4(JAK3):c.1207C>T (p.Arg4...	Likely Pathogenic	T-B+ Severe Combined Immunodeficiency Due To JAK3 Deficiency	2026-10-27	1.0	ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for JAK3 Version 2.3	JAK3

Showing 1 to 1 of 1 rows

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