

Variant: *NM_000536.4(RAG2):c.217C>T (p.Arg73Cys)*

Version: 1.0

CA214218 [↗](#)

36719 (ClinVar) [↗](#)

Gene: RAG2 (HGNC:5897)

Condition: recombinase activating gene 2 deficiency (MONDO:0000573)

Inheritance Mode: Autosomal recessive inheritance

UID: ed88a6c9-e610-46f2-a97f-e3d4667b446b

Approved on: 2024-01-17

Published on: 2024-01-17

HGVS expressions

NM_000536.4:c.217C>T

NM_000536.4(RAG2):c.217C>T (p.Arg73Cys)

NC_000011.10:g.36593952G>A

CM000673.2:g.36593952G>A

NC_000011.9:g.36615502G>A

CM000673.1:g.36615502G>A

NC_000011.8:g.36572078G>A

NG_007573.1:g.9285C>T

NG_033154.1:g.4460G>A

ENST00000527033.6:c.217C>T

ENST00000529083.2:c.217C>T

ENST00000532616.2:c.217C>T

ENST00000311485.8:c.217C>T

ENST00000311485.7:c.217C>T

ENST00000524423.1:n.131+4150C>T

ENST00000529083.1:c.217C>T

ENST00000618712.4:c.217C>T

NM_000536.3:c.217C>T

NM_001243785.1:c.217C>T

NM_001243786.1:c.217C>T

NM_001243785.2:c.217C>T

NM_001243786.2:c.217C>T

Likely Pathogenic

Met criteria codes **5**

PP4 PM3 PM5_Supporting

PM1_Supporting PM2_Supporting

Not Met criteria codes **1**

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 RAG2 Version 1.0.0











[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**



Severe Combined Immunodeficiency Disease VCEP

The c.217C>T (NM_000536.4) variant in RAG2 is a missense variant predicted to cause substitution of Arginine by Cysteine at amino acid 73 (p.Arg73Cys). The filtering allele frequency (the upper threshold of the 95% CI of 2/16256) of the c.217C>T variant in RAG2 is 0.00002132 for African/African American chromosomes by gnomAD v2.1.1 (no homozygous reported), which is lower than the ClinGen SCID VCEP threshold (<0.0000588) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). This variant resides within a region, amino acids 1-383, of RAG2 that is defined as a critical functional domain by the ClinGen SCID VCEP (PMID: 26996199) (PM1_Supporting). PMID: 24481607: Proband compound heterozygous (comp het (R73C/C178X, Pathogenic according to SCID VCEP specifications, 1 pt, PM3_met). NM_000536.4(RAG2):c.218G>A (p.Arg73His), LP according to SCID VCEP specifications, PM5_Supporting. At least one patient with this variant displayed: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5pt) and T-B-NK+ lymphocyte subset profile (0.5pt), totalizing 1 pt, which is highly specific for SCID (PP4, PMID: 20603253). In summary, this variant is classified as Likely Pathogenic for AR SCID. ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PP4, PM1_Supporting, PM3, PM5_Supporting, and PM2_Supporting. (VCEP specifications version 1).

Met criteria codes

PP4			At least one patient with this variant displayed: Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met (0.5pt) and T-B-NK+ lymphocyte subset profile (0.5pt), totalizing 1 pt, which is highly specific for SCID (PP4, PMID: 20603253).
PM3			PMID: 24481607: Proband compound heterozygous (comp het (R73C/C178X, Pathogenic according to SCID VCEP specifications, 1 pt, PM3_met).
PM5_Supporting			NM_000536.4(RAG2):c.218G>A (p.Arg73His), LP according to SCID VCEP specifications, PM5_Supporting.
PM1_Supporting			This variant resides within a region, amino acids 1-383, of RAG2 that is defined as a critical functional domain by the ClinGen SCID VCEP (PMID: 26996199) (PM1_Supporting).
PM2_Supporting			The filtering allele frequency (the upper threshold of the 95% CI of 2/16256) of the c.217C>T variant in RAG2 is 0.00002132 for African/African American chromosomes by gnomAD v2.1.1 (no homozygous reported), which is lower than the ClinGen SCID VCEP threshold (<0.0000588) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
------------	---	---	--

	▼	▼
--	---	---

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.