

Variant: *NM_000448.3(RAG1):c.2095C>T (p.Arg699Trp)*

Version: 1.1

CA219824 [↗](#)

68689 (ClinVar) [↗](#)

Gene: RAG1 ([HGNC:5896](#))

Condition: recombinaase activating gene 1 deficiency ([MONDO:0000572](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 288af6b0-dcff-492f-8fcb-9b924005ad8a

Approved on: 2026/5/6

Published on: 2026/5/21

HGVS expressions

NM_000448.3:c.2095C>T

NM_000448.3(RAG1):c.2095C>T (p.Arg699Trp)

NC_000011.10:g.36575399C>T

CM000673.2:g.36575399C>T

NC_000011.9:g.36596949C>T

CM000673.1:g.36596949C>T

NC_000011.8:g.36553525C>T

NG_007528.1:g.12387C>T

ENST00000697713.1:c.2095C>T

ENST00000697714.1:c.2095C>T

ENST00000697715.1:c.2095C>T

ENST00000299440.6:c.2095C>T

ENST00000299440.5:c.2095C>T

ENST00000534663.1:c.2095C>T

NM_000448.2:c.2095C>T

NM_001377277.1:c.2095C>T

NM_001377278.1:c.2095C>T

NM_001377279.1:c.2095C>T

NM_001377280.1:c.2095C>T

Likely Pathogenic

Met criteria codes **5**

PM1_Supporting

PP4

PM2_Supporting

PS3_Moderate

PM3

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 RAG1 Version 2.1.0

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

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

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000448.3(RAG1):c.2095C>T is a missense variant predicted to cause substitution of Arginine by Tryptophan at amino acid 699 (p.Arg699Trp).The filtering allele frequency (the upper threshold of the 95% CI of 5/1179830) of the c.2095C>T variant in RAG1 is 0.000001320 for European Non-Finnish chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000102) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).This missense variant is located in the core domain (amino acids 387-1011) (PM1_supporting).Patient with SCID (0.5 pt.), genome sequencing conducted (0.5 pt.),T-B-NK+ lymphocyte subset profile (0.5 pt.) Total :1.5 pts. (PMID: 29107076) (PP4). The VDJ recombination activity was found to be 19.3 +/- 1.8 % of WT (mean +/- SE) in a flow cytometry based assay. PMID : 24290284 (PS3_Moderate).The patient (PMID: 21771083) was found heterozygous for R699W & Y1001X (not yet curated by SCID VCEP); p.R699W & p.393fsX402 (not yet curated by SCID VCEP)(PMID: 21184155); homozygous in 3 individuals (PMIDs: 24122031,31503426, 32447396) (Pt.: 1)(PM3). In summary, this variant meets the criteria to be classified as Likely Pathogenic variant for autosomal recessive severe combined immunodeficiency due to RAG1 deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PM1_supporting,PM2_Supporting, PP4,PS3_Moderate,PM3(VCEP specifications version 2.1.0).

Met criteria codes

PM1_Supporting			This missense variant is located in the core domain (amino acids 387-1011) (PM1_supporting).
PP4			Patient with SCID (0.5 pt.), genome sequencing conducted (0.5 pt.),T-B-NK+ lymphocyte subset profile (0.5 pt.) Total :1.5 pts. (PMID: 29107076) (PP4).
PM2_Supporting			The filtering allele frequency (the upper threshold of the 95% CI of 5/1179830) of the c.2095C>T variant in RAG1 is 0.000001320 for European Non-Finnish chromosomes by gnomAD v4, which is lower than the ClinGen SCID VCEP threshold (<0.000102) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).
PS3_Moderate			The VDJ recombination activity was found to be 19.3 +/- 1.8 % of WT (mean +/- SE) in a flow cytometry based assay. PMID : 24290284 (PS3_Moderate)
PM3			The patient (PMID: 21771083) was found heterozygous for R699W & Y1001X (not yet curated by SCID VCEP); p.R699W & p.393fsX402 (not yet curated by SCID VCEP)(PMID: 21184155); homozygous in 3 individuals (PMIDs: 24122031,31503426,32447396) (Pt.:1) (PM3).

Curation History



 ▾

 ▾

Showing 1 to 2 of 2 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.

[ClinGen Terms of Use.](#)

[✕ Powered by BCM's Genboree.](#)