

Variant: NM_000536.4(RAG2):c.3G>A (p.Met1Ile)

Version: 1.0

CA380145362 [↗](#)

2019436 (ClinVar) [↗](#)

Gene: RAG2 ([HGNC:5897](#))

Condition: recombinase activating gene 2 deficiency ([MONDO:0000573](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: ddf7f331-67b6-4a5d-b298-8536f6c07030

Approved on: 2024/3/4

Published on: 2024/3/4

HGVS expressions

NM_000536.4(RAG2):c.3G>A (p.Met1Ile)

NM_000536.4:c.3G>A

NC_000011.10:g.36594166C>T

CM000673.2:g.36594166C>T

NC_000011.9:g.36615716C>T

CM000673.1:g.36615716C>T

NC_000011.8:g.36572292C>T

NG_007573.1:g.9071G>A

NG_033154.1:g.4674C>T

ENST00000527033.6:c.3G>A

ENST00000529083.2:c.3G>A

ENST00000532616.2:c.3G>A

ENST00000311485.8:c.3G>A

ENST00000311485.7:c.3G>A

ENST00000524423.1:n.131+3936G>A

ENST00000527033.5:c.3G>A

ENST00000529083.1:c.3G>A

ENST00000532616.1:c.3G>A

ENST00000618712.4:c.3G>A

NM_000536.3:c.3G>A

NM_001243785.1:c.3G>A

NM_001243786.1:c.3G>A

NM_001243785.2:c.3G>A

NM_001243786.2:c.3G>A

Likely Pathogenic

Met criteria codes **5**

PP4 PM3 PM2_Supporting

PVS1_Supporting PM1_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 RAG2 Version 1.0.0

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

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000536.4(RAG2):c.3G>A is a missense variant predicted to cause substitution of Methionine by Isoleucine at amino acid 1 (p.Met1Ile).This sequence change affects the initiator methionine of the RAG2 mRNA. The next possible initiation codon is at codon 5. This region does not contain known pathogenic/likely pathogenic variants. (PVS1_Supporting).This missense variant is located in the core domain (amino acids 1-383) (PM1_supporting). The variant is absent in gnomAD v4 (PM2_supporting). This variant was found in trans with p.Arg229Gln (classified as pathogenic by SCID VCEP) (1 pt.) (PM3) (Invitae proband; internal lab communication).Patient with SCID (0.5 pt.), SCID gene panel conducted (0.5 pt.),T- B- NK+ by flow cytometry (0.5 pt.); total :1.5 pts (PP4) (Invitae proband; internal lab communication). To our knowledge, this variant has not been reported in the literature in individuals affected with RAG2 related conditions or in functional studies. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for autosomal recessive severe combined immunodeficiency due to RAG2 deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PVS1_Supporting,PM1_supporting,PM2_supporting,PM3,PP4 (VCEP specifications version 1).

Met criteria codes

PP4			Patient with SCID (0.5 pt.), SCID gene panel conducted (0.5 pt.),T- B- NK+ by flow cytometry (0.5 pt.); total :1.5 pts (PP4) (Invitae proband; internal lab communication).
PM3			This variant was found in trans with p.Arg229Gln (classified as pathogenic by SCID VCEP) (1 pt.) (PM3)(Invitae proband; internal lab communication)
PM2_Supporting			The variant is absent in gnomAD v4 (PM2_supporting).
PVS1_Supporting			This sequence change affects the initiator methionine of the RAG2 mRNA. The next possible initiation codon is at codon 5. This region does not contain known pathogenic/likely pathogenic variants. (PVS1_Supporting).
PM1_Supporting			This missense variant is located in the core domain (amino acids 1-383) (PM1_supporting).

Curation History [↗](#)



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