

Variant: *NM_000448.3(RAG1):c.775del (p.Ser259fs)*

Version: 1.0

CA10581303 [↗](#)

235411 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: d019dc02-6ae2-4e39-a212-455368ee11ca

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HGVS expressions

NM_000448.3:c.775del

NM_000448.3(RAG1):c.775del (p.Ser259fs)

NC_000011.10:g.36574079del

CM000673.2:g.36574079del

NC_000011.9:g.36595629del

CM000673.1:g.36595629del

NC_000011.8:g.36552205del

NG_007528.1:g.11067del

ENST00000697713.1:c.775del

ENST00000697714.1:c.775del

ENST00000697715.1:c.775del

ENST00000299440.6:c.775del

ENST00000299440.5:c.775del

ENST00000534663.1:c.775del

NM_000448.2:c.775del

NM_001377277.1:c.775del

NM_001377278.1:c.775del

NM_001377279.1:c.775del

NM_001377280.1:c.775del

Pathogenic

Met criteria codes **3**

PVS1

PM2_Supporting

PM3_Supporting

Not Met criteria codes **1**

PP4

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 1.0.0*

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

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

Severe Combined Immunodeficiency Disease VCEP

The nonsense variant NM_000448.3(RAG1):c.775del (p.Ser259AlafsTer5) occurs in exon 2 of 2 (the only coding exon of RAG1) and is not predicted to result in nonsense mediated decay but does truncate 75% of the protein, including the entirety of the core domain (amino acids 387-1011) which is critical to protein function (PMID: 26996199; PVS1). This variant is absent from gnomADv2.1.1 (PM2_Supporting). It has been reported homozygous in one patient with Omenn syndrome (PM3_supporting) with insufficient information to determine that the patient's phenotype is highly specific to recombinae activating gene 1 deficiency (PP4_NotMet). In summary, this variant meets the criteria to be classified as pathogenic for recombinae activating gene 1 deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP. Criteria applied: PVS1, PM3_Supporting, and PM2_Supporting. (VCEP specifications version 1).

Met criteria codes

PVS1			The nonsense variant NM_000448.3(RAG1):c.775del (p.Ser259AlafsTer5) occurs in exon 2 of 2 (the only coding exon of RAG1) and is not predicted to result in nonsense mediated decay but does truncate 75% of the protein, including the entirety of the core domain (amino acids 387-1011) which is critical to protein function (PMID: 26996199; PVS1).
PM2_Supporting			This variant is absent from gnomADv2.1.1 (PM2_Supporting).
PM3_Supporting			P28 of PMID: 28769923 is homozygous for this variant (0.5pt; PM3_supporting).

Not Met criteria codes

PP4			Omenn patient P28 of PMID: 28769923 had insufficient information for PP4.
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Curation History



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