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Variant: NM_000536.4(RAG2):c.35T>C (p.Ile12Thr)

Version: 1.0

CA5950633

573475 (ClinVar)

Gene: RAG2 (HGNC:5897)
Condition: recombinase activating gene 2 deficiency (MONDO:0000573)
Inheritance Mode: Autosomal recessive inheritance
UUID: ed04ab15-ccd2-4f7e-b32a-40003882b24f
Approved on: 2024/6/10
Published on: 2024/6/10

HGVS expressions

NM_000536.4:c.35T>C
NM_000536.4(RAG2):c.35T>C (p.Ile12Thr)
NC_000011.10:g.36594134A>G
CM000673.2:g.36594134A>G
NC_000011.9:g.36615684A>G
CM000673.1:g.36615684A>G
NC_000011.8:g.36572260A>G
NG_007573.1:g.9103T>C
NG_033154.1:g.4642A>G
ENST00000527033.6:c.35T>C
ENST00000529083.2:c.35T>C
ENST00000532616.2:c.35T>C
ENST00000311485.8:c.35T>C
ENST00000311485.7:c.35T>C
ENST00000524423.1:n.131+3968T>C
ENST00000527033.5:c.35T>C
ENST00000529083.1:c.35T>C
ENST00000618712.4:c.35T>C
NM_000536.3:c.35T>C
NM_001243785.1:c.35T>C
NM_001243786.1:c.35T>C
NM_001243785.2:c.35T>C
NM_001243786.2:c.35T>C

Uncertain Significance

Met criteria codes 1

PM1_Supporting

Not Met criteria codes 1

PM2

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**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

NM_000536.4(RAG2):c.35T>C is a missense variant predicted to cause substitution of Isoleucine by Threonine at amino acid 12 (p.Ile12Thr).This missense variant is located in the core domain (amino acids 1-383) (PM1_supporting). The highest population minor allele frequency in gnomAD v4 is 0.001750 (151/75030) in African/African American population. (PM2_Supporting, BS1 and BA1 are not met). 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: PM1_supporting (VCEP specifications version 1).

Met criteria codes

PM1_Supporting	✔	This missense variant is located in the core domain (amino acids 1-383) (PM1_supporting).

Not Met criteria codes

PM2	✖	The highest population minor allele frequency in gnomAD v4 is 0.001750 (151/75030) in African/African American population. (PM2_Supporting, BS1 and BA1 are not met)

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000536.4(RAG2):c.35T>C (p.Ile12T...	Uncertain Significance	Recombinase Activating Gene 2 Deficiency	2024-06-10	1.0	ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RAG2 Version 1.0.0	RAG2

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