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Variant: NM_001369369.1(FOXN1):c.1376C>A (p.Ser459Ter)

Version: 1.0

CA8459509

837219 (ClinVar)

Gene: FOXN1 (HGNC:8456)
Condition: T-cell immunodeficiency, congenital alopecia, and nail dystrophy (MONDO:0011132)
Inheritance Mode: Semidominant inheritance
UUID: 40f6c095-62f8-4931-9615-0009ab2685e2
Approved on: 2025/4/25
Published on: 2025/7/14

HGVS expressions

NM_001369369.1(FOXN1):c.1376C>A (p.Ser459Ter)
NM_001369369.1:c.1376C>A
NC_000017.11:g.28534947C>A
CM000679.2:g.28534947C>A
NC_000017.10:g.26861965C>A
CM000679.1:g.26861965C>A
NC_000017.9:g.23886092C>A
NG_007260.1:g.16007C>A
ENST00000577936.2:c.1376C>A
ENST00000579795.6:c.1376C>A
ENST00000226247.2:c.1376C>A
ENST00000481916.6:c.*1195+69104G>T
ENST00000579795.5:c.1376C>A
NM_003593.2:c.1376C>A
NM_003593.3:c.1376C>A

Pathogenic

Met criteria codes 3

PVS1 PM5_Supporting PM2_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 FOXN1 Version 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The NM_001369369.1:c.1376C>A variant in FOXN1 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 8/9 leading to nonsense mediated decay (PVS1). The highest population minor allele frequency in gnomAD v4.1.0 is 8.475e-7

(1/1180000 alleles) in European (non-Finnish) population, which is lower than the SCID-VCEP threshold (<0.00002412) for PM2_Supporting. No homozygous individual has been observed (PM2_Supporting). A pathogenic variant p.Gln474Ter curated by the SCID VCEP causes premature termination codon in the same exon and downstream to the variant under assessment (PM5_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for SCID. ACMG/AMP criteria applied, as specified by the ClinGen SCID-VCEP: PVS1, PM2_Supporting, PM5_Supporting. (VCEP specifications version 2.0.0)

Met criteria codes

PVS1	✔	The c.1376C>A (NM_001369369.1) variant in FOXN1 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 8/9 leading to nonsense mediated decay.
PM5_Supporting	✔	A pathogenic variant p.Gln474Ter curated by the SCID VCEP causes premature termination codon in the same exon and downstream to the variant under assessment (1pt). 1pt in total for PM5, PM5_Supporting is met.
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.0 is 8.475e-7 (1/1180000 alleles) in European (non-Finnish) population, which is lower than the SCID-VCEP threshold (<0.00002412) for PM2_Supporting. No homozygous individual has been observed in the gnomAD v4.1.0. (PM2_Supporting)

Curation History

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