

Variant: NM_001369369.1(FOXN1):c.933_936dup
(p.Asp313fs)

Version: 1.0

CA915949637 [↗](#)

827574 (ClinVar) [↗](#)

Gene: FOXN1 ([HGNC:8456](#))

Condition: T-cell immunodeficiency, congenital alopecia, and nail dystrophy ([MONDO:0011132](#))

Inheritance Mode: Semidominant inheritance

UUID: 3fee475c-7628-4c86-a0c7-ffcd348b9fe7

Approved on: 2024/7/29

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HGVS expressions

NM_001369369.1:c.933_936dup

NM_001369369.1(FOXN1):c.933_936dup (p.Asp313fs)

NC_000017.11:g.28534336_28534339dup

CM000679.2:g.28534336_28534339dup

NC_000017.10:g.26861354_26861357dup

CM000679.1:g.26861354_26861357dup

NC_000017.9:g.23885481_23885484dup

NG_007260.1:g.15396_15399dup

ENST00000577936.2:c.933_936dup

ENST00000579795.6:c.933_936dup

ENST00000226247.2:c.933_936dup

ENST00000481916.6:c.*1195+69713_1195+69716dup

ENST00000579795.5:c.933_936dup

NM_003593.2:c.933_936dup

NM_003593.3:c.933_936dup

Pathogenic

Met criteria codes 3

PVS1

PP4

PM2_Supporting

Not Met criteria codes 3

PM3

PS3

PS4

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 1.0.0

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

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

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The NM_001369369.1(FOXN1):c.933_936dup (p.Asp313ThrfsTer?) frameshift variant in exon 7, of 9, results in a premature stop codon in exon 8, which is predicted to cause NMD (PVS1). The variant was detected by exome sequencing with Sanger confirmation in one patient (Pt 1) who is compound heterozygous with c.1089_1103del (PMID: 31566583). The patient has normal hair and nails but T-B+NK+ SCID. They had Undetectable TRECs, at 3 months there were low CD3 31 cells/uL (0.5pt), and CD8 3 cells/uL, with NK 188 cells/uL, CD19+ 2159 cells/uL (PP4). In summary this variant meets criteria to be classified as pathogenic for semidominant T-cell immunodeficiency, congenital alopecia, and nail dystrophy due to FOXN1 deficiency based on the ACMG/AMP criteria applied: PVS1, PM2_supporting, and PP4 as specified by the ClinGen SCID VCEP FOXN1 subgroup.

Met criteria codes

PVS1			This frameshift variant in exon 7, of 9, results in a premature stop codon in exon 8, which is predicted to cause NMD (PVS1).
PP4			The variant was detected by exome sequencing with Sanger confirmation in one patient (Pt 1) with normal hair and nails but T-B+NK+ SCID. They had Undetectable TRECs, at 3 months CD3 31 cells/uL (2500-5500) (0.5pt), CD8 3 (500-1700), NK 188 (170-1100), CD19+ 2159 (300-2000), (PMID: 31566583; PP4).
PM2_Supporting			This variant is absent from gnomADv4.0 (PM2_supporting).

Not Met criteria codes

PM3			Pt1 is compound heterozygous with c.1089_1103del which has not yet been classified by the SCID VCEP (PMID: 31566583).
PS3			Expression vectors containing Foxn1 variants were transfected into HeLa cells along with the β5t-luciferase reporter construct, a well-defined transcriptional target of Foxn1. This variant resulted in 0.90% activity in the reporter assay compared to WT (PMID: 37419334). This evidence is not considered here since this variant was used as a Pathogenic control for this assay.
PS4			One heterozygous case has been reported (SCV001579576.3) with a consistent phenotype 0.25pt (PS4_NotMet).

Curation History 

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001369369.1(FOXN1):c.933_936du...	Pathogenic	T-Cell Immunodeficiency, Congenital Alopecia, And Nail Dystrophy	2024-07-29	1.0	ClinGen Severe Combined Immunodeficiency Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for FOXN1 Version 1.0.0	FOXN1

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