

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: 2024-07-29

Published on: 2024-07-29

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

PP4 **PM2_Supporting** **PVS1**

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

- | | | | |
|-----------------------|---|---|---|
| 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). |
| 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). |

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 β 5t-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

Showing 1 to 1 of 1 rows



The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

[ClinGen Terms of Use.](#)
⌘ [Powered by BCM's Genboree.](#)