Variant: NR_003051.4(RMRP):n.244A>C

Version: 1.4

CA464450288

553173 (ClinVar)

Gene: N/A
Condition: cartilage-hair hypoplasia (MONDO:0009595)
Inheritance Mode: Autosomal recessive inheritance
UUID: 653077d3-181e-4003-b68e-a447c756e041
Approved on: 2025-06-10
Published on: 2026-02-06

HGVS expressions

NR_003051.4:n.244A>C
NR_003051.4(RMRP):n.244A>C
NC_000009.12:g.35657776T>G
CM000671.2:g.35657776T>G
NC_000009.11:g.35657773T>G
CM000671.1:g.35657773T>G
NC_000009.10:g.35647773T>G
NG_017041.1:g.5243A>C
NG_033120.1:g.4487T>G
NR_003051.3:n.243A>C

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PM3 PM2_Supporting PS1_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 RMRP Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The NC_000009.12:g.35657776T>G is present in a frequency of 0.000006567 Grpmax filtering AF with only 1 allele in 152268, which is below the PM2_Supporting threshold that the SCID VCEP has established, therefore meeting this criterion. Internal data: at least one patient has presented with metaphyseal dysplasia (disproportionate short stature + radiographic evidence) (+1.0), skeletal dysplasia gene panel or WES/WGS conducted with no alternative genetic diagnosis (+1.0) and hypotrichosis (+0.5) reaching a total of 2.5 points. Therefore PP4_Moderate is met. Internal data: this variant has been confirmed in trans with NR_003051.3:n.196C>T (classified Pathogenic by VCEP +1.0) in a proband with the short disproportionate stature, rhizomelic dysplasia, and sparse light hair. Therefore PM3 is met. Finally, this variant (n.244A>C) is located at position 244, which is the same nucleotide that another variant has been classified as Likely

Pathogenic in position 244 (n.244A>G), meeting PS1_Supporting. In summary, this variant is classified as Likely Pathogenic for Autosomal Recessive Cartilage Hair Hypoplasia based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PM2_Supporting, PS1_Supporting, PM3, PP4_Moderate (SCID VCEP RMRP specifications version 1).

Met criteria codes

PP4_Moderate	✔	No published cases were identified. Internal communication - Invitae/Labcorp - at least one patient has presented with metaphyseal dysplasia (disproportionate short stature + radiographic evidence) (+1.0), skeletal dysplasia gene panel or WES/WGS conducted with no alternative genetic diagnosis (+1.0) and hypotrichosis (+0.5) reaching a total of 2.5 points. Therefore PP4_Moderate is met.
PM3	✔	Internal communication - Invitae/Labcorp - NR_003051.3:n.243A>C (NR_003051.4:n.244A>C): we have seen this variant confirmed in trans with NR_003051.3:n.196C>T (classified path by VCEP +1.0) in proband with indication of short disproportionate stature, rhizomelic dysplasia, sparse light hair. No other clinical information provided. 358 gene skeletal dysplasia panel ordered. Single heterozygous VUS in ANO5 and COL2A1 genes were also identified (both genes are associated with autosomal dominant skeletal dysplasias) but neither of these variants have any case reports or literature that I can see, we did not consider these as likely alternate causes of disease.
PM2_Supporting	✔	This variant is present in a frequency of 0.000006567 Grpmax filtering AF with only 1 allele in 152268 which is below the PM2_Supporting threshold that the SCID VCEP has established. Therefore this code is applicable PM2_Supporting.
PS1_Supporting	✔	This variant (n.244A>C) is located at position 244, which is the same nucleotide that another variant has been classified as Likely Pathogenic in position 244 (n.244A>G), meeting PS1_Supporting.

Curation History

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