The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NR_003051.4(RMRP):n.264G>T

Version: 1.2

CA257181

14209 (ClinVar)

Gene: RMRP (HGNC:6023)
Condition: cartilage-hair hypoplasia (MONDO:0009595)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7fb7723f-2d30-49a6-9690-e58f442e90a9
Approved on: 2025-09-30
Published on: 2025-12-09

HGVS expressions

NR_003051.4:n.264G>T
NR_003051.4(RMRP):n.264G>T
NC_000009.12:g.35657756C>A
CM000671.2:g.35657756C>A
NC_000009.11:g.35657753C>A
CM000671.1:g.35657753C>A
NC_000009.10:g.35647753C>A
NG_017041.1:g.5263G>T
NG_033120.1:g.4467C>A
NR_003051.3:n.263G>T

Pathogenic

Met criteria codes 3

PM3_Very Strong | PP1 | PP4

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 RMRP Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

This variant is present in gnomAD v.4 at a Total allele frequency of 0.00003793, which is lower than the PM2_supporting threshold 0.0000447. while in the subgroup Finnish European, the allele frequency is 0.000552 [24/43478], which is higher than the threshold of 0.0000447. Therefore, the PM2_supporting was not met. At least one patient presented Methapyseal dysplasia (+1.0 points) and hypotrichosis (+0.5 points)(1.5 points, PP4, PMID: 11207361). This variant is reported in trans with the variant (70A>g) in 6 independent families (+1.0 points each), reaching a total score of 6.0, and PM3_VeryStrong is met (PMID: 11207361). A multiple-case family with this variant in trans with n.70A>C is reported with two affected siblings, meeting PP1 (PMID: 11207361). In summary, this variant meets the

criteria to be classified as Pathogenic for Autosomal recessive Cartilage Hair Hypoplasia based on the ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP: PM3_VeryStrong, PP4, and PP1 (VCEP specifications version 1).

Met criteria codes

PM3_Very Strong	✔	This variant is reported in trans with the variant (70A>g) in 6 patients (+1.0 points each). The total score is 6 meeting this criterion PM3_VeryStrong. PMID: 11207361
PP1	✔	A multiple-case family with this variant in trans with n.70A>C is reported with two affected siblings. Therefore this criterion is met at default strength.
PP4	✔	At least one patient presented Methapyseal dysplasia (+1.0 points) and hypotrichosis (+0.5 points) and therefore this criterion is met at default strength (PMID: 11207361).

Not Met criteria codes

PM2	✖	This variant is present in gnomAD v.4 at a Total allele frequency of 0.00003793, which is lower than the PM2_supporting threshold 0.0000447. while in the subgroup Finnish European, the allele frequency is 0.000552 [24/43478], which is higher than the threshold of 0.0000447. Therefore, the PM2_supporting was not met. NOTE: gnomAD does not provide GroupMax Filtering AF for this variant, therefore for this curation, we use the total allele frequency.

Curation History

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