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: NM_001033855.3(DCLRE1C):c.82G>C (p.Ala28Pro)

Version: 1.0

CA376065726

2136853 (ClinVar)

Gene: DCLRE1C (HGNC:64421)
Condition: severe combined immunodeficiency due to DCLRE1C deficiency (MONDO:0011225)
Inheritance Mode: Autosomal recessive inheritance
UUID: efb9cd5b-4386-4c4f-bb04-8543325a5c80
Approved on: 2024/1/23
Published on: 2024/1/23

HGVS expressions

NM_001033855.3(DCLRE1C):c.82G>C (p.Ala28Pro)
NM_001033855.3:c.82G>C
NC_000010.11:g.14953929C>G
CM000672.2:g.14953929C>G
NC_000010.10:g.14995928C>G
CM000672.1:g.14995928C>G
NC_000010.9:g.15035934C>G
NG_007276.1:g.5167G>C
ENST00000378241.6:c.82G>C
ENST00000456122.2:c.82G>C
ENST00000489161.2:c.82G>C
ENST00000492201.6:c.82G>C
ENST00000697047.1:c.82G>C
ENST00000697070.1:c.82G>C
ENST00000697071.1:c.82G>C
ENST00000697072.1:c.82G>C
ENST00000697073.1:c.82G>C
ENST00000697074.1:c.82G>C
ENST00000697075.1:c.82G>C
ENST00000697076.1:c.82G>C
ENST00000697077.1:c.82G>C
ENST00000697078.1:c.82G>C
ENST00000697080.1:c.82G>C
ENST00000697081.1:c.82G>C
ENST00000697082.1:c.82G>C
ENST00000697083.1:c.82G>C
ENST00000697084.1:c.82G>C
ENST00000697085.1:c.82G>C
ENST00000697087.1:c.82G>C
ENST00000697088.1:c.82G>C
ENST00000697089.1:c.82G>C
ENST00000697090.1:n.5G>C
ENST00000697091.1:n.143G>C
ENST00000378278.7:c.82G>C
ENST00000357717.6:c.-123G>C
ENST00000378241.5:c.-491G>C
ENST00000378246.6:c.-208G>C

ENST00000378249.5:c.-156G>C
ENST00000378254.5:c.-410G>C
ENST00000378255.5:c.-732G>C
ENST00000378258.5:c.-364G>C
ENST00000378278.6:c.82G>C
ENST00000378289.8:c.82G>C
ENST00000396817.6:c.-686G>C
ENST00000418843.5:c.-447G>C
ENST00000456122.1:c.-615G>C
NM_001033855.2:c.82G>C
NM_001033857.2:c.-364G>C
NM_001033858.2:c.-686G>C
NM_001289076.1:c.-123G>C
NM_001289077.1:c.-410G>C
NM_001289078.1:c.-156G>C
NM_001289079.1:c.-732G>C
NM_022487.3:c.-208G>C
NR_110297.1:n.504G>C
NM_001350965.1:c.82G>C
NM_001350966.1:c.-156G>C
NM_001350967.1:c.-364G>C
NR_146960.1:n.504G>C
NR_146961.1:n.504G>C
NR_146962.1:n.504G>C
NM_001033857.3:c.-364G>C
NM_001033858.3:c.-686G>C
NM_001289076.2:c.-123G>C
NM_001289077.2:c.-410G>C
NM_001289078.2:c.-156G>C
NM_001289079.2:c.-732G>C
NM_001350965.2:c.82G>C
NM_001350966.2:c.-156G>C
NM_001350967.2:c.-364G>C
NM_022487.4:c.-208G>C
NR_110297.2:n.168G>C
NR_146961.2:n.168G>C

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP4_Moderate
PM2_Supporting PS3_Moderate

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 DCLRE1C Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Severe Combined Immunodeficiency Disease VCEP

The c.82G>C(NM_001033855.3) variant in DCLRE1C is a missense variant predicted to cause substitution of Alanine by Proline at amino acid 28 (p.Ala28Pro). This variant is absent from gnomAD v4 (PM2_Supporting). At least one patient with this variant displayed Decreased V(D)J recombination 0.5pts + Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met 0.5 pts. + T−B−NK+ 0.5pts + Increased cellular radiosensitivity 0.5pts. The total is 2 points, which is highly specific for SCID (PP4_Moderate, PMIDs 19953608 and 25917813). The patient is homozygous, 0.5pts. PM3_Supporting. Activity levels in % of WT activity = Recombination: Mean (SD): 3.00 (0.15) and DNA repair (36h after IR): Mean (SD): 5.13 (11.95). Both values are lower than our established threshold for abnormal results (defined as <25% of wild-type activity). Thus, PS3 is Met at a moderate level(PMID: 25917813). In summary, this variant is classified as a Likely Pathogenic for autosomal recessive SCID based on ACMG/AMP criteria applied, as specified by the ClinGen SCID VCEP (specification version 1.0): PM2_Supporting, PP4_Moderate, PM3_Supporting, and PS3_Moderate.

Met criteria codes

PM3_Supporting	✔	PMID: 25917813: This patient is homozygous, 0.5pts. PM3_Supporting.
PP4_Moderate	✔	The same patient is described in two reports (PMIDs 19953608 and 25917813): Decreased V(D)J recombination 0.5pts + Diagnostic criteria for SCID/Leaky SCID/Omenn syndrome met 0.5 pts. + T−B−NK+ 0.5pts + Increased cellular radiosensitivity 0.5pts. Total is 2 points, PP4_Moderate.
PM2_Supporting	✔	This variant is absent from gnomAD v4.
PS3_Moderate	✔	Activity levels in % of WT activity = Recombination: Mean (SD): 3.00 (0.15) and DNA repair (36h after IR): Mean (SD): 5.13 (11.95). Both values are lower than our established threshold for abnormal results (defined as <25% of wild-type activity). Thus, PS3 is Met at a moderate level(PMID: 25917813).

Curation History

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