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_177438.3(DICER1):c.1509G>C (p.Glu503Asp)

Version: 2.0

CA390885360

1487846 (ClinVar)

Gene: DICER1 (HGNC:23405)
Condition: DICER1-related tumor predisposition (MONDO:0100216)
Inheritance Mode: Autosomal dominant inheritance
UUID: c256aaa7-0312-4848-81dd-ad5c0af94b04
Approved on: 2025/2/25
Published on: 2025/6/4

HGVS expressions

NM_177438.3:c.1509G>C
NM_177438.3(DICER1):c.1509G>C (p.Glu503Asp)
NC_000014.9:g.95117622C>G
CM000676.2:g.95117622C>G
NC_000014.8:g.95583959C>G
CM000676.1:g.95583959C>G
NC_000014.7:g.94653712C>G
NG_016311.1:g.44801G>C
ENST00000529720.2:c.1509G>C
ENST00000531162.7:c.1509G>C
ENST00000674628.2:c.1509G>C
ENST00000675540.2:c.1509G>C
ENST00000696733.1:c.1509G>C
ENST00000696734.1:c.1509G>C
ENST00000696736.1:c.1509G>C
ENST00000696737.1:c.1509G>C
ENST00000696920.1:n.1772G>C
ENST00000696921.1:n.2615G>C
ENST00000696922.1:n.1918G>C
ENST00000696923.1:c.1509G>C
ENST00000696924.1:c.1509G>C
ENST00000696925.1:n.1918G>C
ENST00000696927.1:n.1112G>C
ENST00000696928.1:n.1706G>C
ENST00000343455.8:c.1509G>C
ENST00000393063.6:c.1509G>C
ENST00000526495.6:c.1509G>C
ENST00000532939.3:c.1509G>C
ENST00000556045.6:c.1509G>C
ENST00000674628.1:c.1509G>C
ENST00000675995.1:c.1509G>C
ENST00000343455.7:c.1509G>C
ENST00000393063.5:c.1509G>C
ENST00000526495.5:c.1509G>C
ENST00000527414.5:c.1509G>C
ENST00000532458.1:n.213G>C
ENST00000541352.5:c.1509G>C

NM_001195573.1:c.1509G>C
NM_001271282.2:c.1509G>C
NM_001291628.1:c.1509G>C
NM_030621.4:c.1509G>C
NM_177438.2:c.1509G>C
NM_001271282.3:c.1509G>C
NM_001291628.2:c.1509G>C
NM_001395677.1:c.1509G>C
NM_001395678.1:c.1509G>C
NM_001395679.1:c.1509G>C
NM_001395680.1:c.1509G>C
NM_001395682.1:c.1509G>C
NM_001395683.1:c.1509G>C
NM_001395684.1:c.1509G>C
NM_001395685.1:c.1509G>C
NM_001395686.1:c.1227G>C
NM_001395687.1:c.1104G>C
NM_001395688.1:c.1104G>C
NM_001395689.1:c.1104G>C
NM_001395690.1:c.1104G>C
NM_001395691.1:c.942G>C
NM_001395692.1:c.1509G>C
NM_001395693.1:c.1509G>C
NM_001395694.1:c.1509G>C
NM_001395695.1:c.1509G>C
NM_001395696.1:c.1104G>C
NM_001395697.1:c.-60G>C
NM_001395698.1:c.1104G>C
NR_172715.1:n.1927G>C
NR_172716.1:n.1854G>C
NR_172717.1:n.2021G>C
NR_172718.1:n.2021G>C
NR_172719.1:n.1854G>C
NR_172720.1:n.1854G>C

Likely Pathogenic

Met criteria codes 5

PS4_Supporting PM2_Supporting PS3 PP1 PP3

Not Met criteria codes 16

PVS1 BS2 BS1 BS4 BS3 BP4 BP2 BP7 PS1 PS2 BA1 PP4 PM6 PM1 PM5 PM4

Evidence Links 0

Expert Panel

DICER1 and miRNA-Processing Gene VCEP

Criteria Specification Information

Criteria Specification: *ClinGen DICER1 and miRNA-Processing Gene Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for DICER1 Version 1.3.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

DICER1 and miRNA-Processing Gene VCEP

NM_177438.2(DICER1):c.1509G>C variant in DICER1 is a missense variant predicted to cause substitution of glutamate by aspartate at amino acid 503 (p.Glu503Asp). This variant received a total of 1 phenotype point across 1 unrelated proband/family meeting DICER1 VCEP phenotype specificity scoring criteria of 1-1.5 points (PS4_Supporting; Internal lab data: Invitae). The variant has been reported to segregate with DICER1 phenotypes in 2 family members separated by 4 meioses from 1 family (PP1_Supporting; Internal lab contributors). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). Sequencing of RNA from patients showed an out-of-frame impact on splicing, indicating that this variant impacts protein function (PS3; Internal lab contributor: Invitae). The splice site predictors MaxEntScan and SpliceAI indicate that the variant impacts splicing, evidence that correlates with impact to DICER1 function (PP3). In summary, this variant meets the criteria to be classified as Likely Pathogenic for DICER1 syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen DICER1 VCEP: PS4_Supporting, PP1, PM2_Supporting, PS3, PP3 (Bayesian Points: 8; VCEP specifications version 1.3.0; 02/25/2025).

Met criteria codes

PS4_Supporting	✔	This variant received a total of 1 phenotype point across 1 unrelated proband/family meeting DICER1 VCEP phenotype specificity scoring criteria of 1-1.5 points
PM2_Supporting	✔	Absent in gnomAD v4.1.0 with good coverage
PS3	✔	Sequencing of RNA from patients showed an out-of-frame impact on splicing, indicating that this variant impacts protein function (PS3; Internal lab contributor: Invitae).
PP1	✔	The variant has been reported to segregate with DICER1 phenotypes in 2 family members separated by 4 meioses from 1 family (PP1_Supporting; Internal lab contributors).
PP3	✔	Last nt of exon has concordant splicing impact for SpliceAI and MaxEntScan

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Not Met criteria codes

PVS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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