

Variant: NM_030621.4(DICER1):c.878_881del (p.Arg293fs)

Version: 1.0

CA10586464 [↗](#)

254355 (ClinVar) [↗](#)

Gene: DICER1 ([HGNC:23405](#))
Condition: dicer1 syndrome ([MONDO:0017288](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: b6047466-f62a-4f0c-845a-8fe2dba71e1c
Approved on: 2022/5/18
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HGVS expressions

NM_030621.4:c.878_881del
NM_030621.4(DICER1):c.878_881del (p.Arg293fs)
NC_000014.9:g.95126603_95126606del
CM000676.2:g.95126603_95126606del
NC_000014.8:g.95592940_95592943del
CM000676.1:g.95592940_95592943del
NC_000014.7:g.94662693_94662696del
NG_016311.1:g.35818_35821del
ENST00000529720.2:c.878_881del
ENST00000531162.7:c.878_881del
ENST00000674628.2:c.878_881del
ENST00000675540.2:c.878_881del
ENST00000696733.1:c.878_881del
ENST00000696734.1:c.878_881del
ENST00000696736.1:c.878_881del
ENST00000696737.1:c.878_881del
ENST00000696921.1:n.1984_1987del
ENST00000696922.1:n.1287_1290del
ENST00000696923.1:c.878_881del
ENST00000696924.1:c.878_881del
ENST00000696925.1:n.1287_1290del
ENST00000696927.1:n.481_484del
ENST00000696928.1:n.1075_1078del
ENST00000343455.8:c.878_881del
ENST00000393063.6:c.878_881del
ENST00000526495.6:c.878_881del
ENST00000532939.3:c.878_881del
ENST00000556045.6:c.878_881del
ENST00000674628.1:c.878_881del
ENST00000675995.1:c.878_881del
ENST00000343455.7:c.878_881del
ENST00000393063.5:c.878_881del
ENST00000526495.5:c.878_881del
ENST00000527414.5:c.878_881del
ENST00000541352.5:c.878_881del
NM_001195573.1:c.878_881del
NM_001271282.2:c.878_881del

	NM_001291628.1:c.878_881del
	NM_177438.2:c.878_881del
	NM_001271282.3:c.878_881del
	NM_001291628.2:c.878_881del
	NM_177438.3:c.878_881del
	NM_001395677.1:c.878_881del
	NM_001395678.1:c.878_881del
	NM_001395679.1:c.878_881del
	NM_001395680.1:c.878_881del
	NM_001395682.1:c.878_881del
	NM_001395683.1:c.878_881del
	NM_001395684.1:c.878_881del
	NM_001395685.1:c.878_881del
	NM_001395686.1:c.596_599del
	NM_001395687.1:c.473_476del
	NM_001395688.1:c.473_476del
	NM_001395689.1:c.473_476del
	NM_001395690.1:c.473_476del
	NM_001395691.1:c.311_314del
	NM_001395692.1:c.878_881del
	NM_001395693.1:c.878_881del
	NM_001395694.1:c.878_881del
	NM_001395695.1:c.878_881del
	NM_001395696.1:c.473_476del
	NM_001395697.1:c.-691_-688del
	NM_001395698.1:c.473_476del
	NM_001395699.1:c.878_881del
	NM_001395700.1:c.878_881del
	NR_172715.1:n.1092_1095del
	NR_172716.1:n.1223_1226del
	NR_172717.1:n.1390_1393del
	NR_172718.1:n.1390_1393del
	NR_172719.1:n.1223_1226del
	NR_172720.1:n.1223_1226del

Pathogenic

Met criteria codes 4

PM2_Supporting

PP4

PS4_Supporting

PVS1

Not Met criteria codes 9

BA1

BP2

BS1

BS3

PP1

PS2

PS3

PM1

PM6

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

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

DICER1 and miRNA-Processing Gene VCEP

The NM_177438.2:c.878_881del (p.Arg293fs) variant in DICER1 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 7/27 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant received a total of 1 phenotype point across 1 proband meeting DICER1 VCEP phenotype specificity scoring criteria of 1-1.5 points (PS4_Supporting, PMID: 26925222). This individual was found to have a somatic second hit in a recognized DICER1 hotspot codon on tumor sequencing, which is highly specific for DICER1 syndrome (PP4, PMID: 26925222). This variant is absent from gnomAD v2.1.1 and v3.1.1 (non-cancer) (PM2_Supporting). In summary, this variant meets the criteria to be classified as **PATHOGENIC** for DICER1 syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen DICER1 VCEP: PVS1, PS4_Supporting, PP4, PM2_Supporting. (Bayesian Points: 11; VCEP specifications version 1; 02/11/2022)

Met criteria codes

PM2_Supporting			Absent from gnomAD 2.1.1 and 3.1.1 (non-cancer) with >20x coverage
PP4			Hotspot second hit variant identified in proband's PPB was c.5425G>A (p.G1809R) (PMID: 26925222)
PS4_Supporting			Germline variant in child with PPB Type II; inherited (Study ID 37 Table S3, S5, S6) – high specificity. 1 pt for proband with high-specificity phenotype (PMID: 26925222, NCI, IPPBR, Ambry)
PVS1			Predicted to undergo NMD, stop codon 5’ of p.P1850; (p.Arg293IlefsTer4)

Not Met criteria codes

BA1			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
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No studies identified.
PP1			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
PS3			No studies identified.
PM1			

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

Curation History ↗		
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