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Variant: NM_177438.2(DICER1):c.3019C>T (p.Gln1007Ter)

Version: 1.0

CA390878423

429113 (ClinVar)

Gene: DICER1 (HGNC:23405)
Condition: dicer1 syndrome (MONDO:0017288)
Inheritance Mode: Autosomal dominant inheritance
UUID: a06f071b-cc61-42ee-8dcd-c4aad03f7af7
Approved on: 2022/5/18
Published on: 2022/7/8

HGVS expressions

NM_177438.2(DICER1):c.3019C>T (p.Gln1007Ter)
NM_177438.2:c.3019C>T
NC_000014.9:g.95105752G>A
CM000676.2:g.95105752G>A
NC_000014.8:g.95572089G>A
CM000676.1:g.95572089G>A
NC_000014.7:g.94641842G>A
NG_016311.1:g.56671C>T
ENST00000529720.2:c.3019C>T
ENST00000531162.7:c.3019C>T
ENST00000674628.2:c.3019C>T
ENST00000675540.2:c.3019C>T
ENST00000696733.1:c.3019C>T
ENST00000696734.1:c.3019C>T
ENST00000696736.1:c.3019C>T
ENST00000696737.1:c.3019C>T
ENST00000696738.1:n.907C>T
ENST00000696920.1:n.3282C>T
ENST00000696921.1:n.4125C>T
ENST00000696922.1:n.3428C>T
ENST00000696923.1:c.3019C>T
ENST00000696924.1:c.3019C>T
ENST00000696925.1:n.3428C>T
ENST00000343455.8:c.3019C>T
ENST00000393063.6:c.3019C>T
ENST00000526495.6:c.3019C>T
ENST00000532939.3:c.3019C>T
ENST00000556045.6:c.3019C>T
ENST00000675540.1:c.841C>T
ENST00000675995.1:c.*1335C>T
ENST00000343455.7:c.3019C>T
ENST00000393063.5:c.3019C>T
ENST00000526495.5:c.3019C>T
ENST00000527414.5:c.3019C>T
ENST00000541352.5:c.3019C>T
ENST00000554367.1:n.228C>T
ENST00000556045.5:c.-211C>T

NM_001195573.1:c.3019C>T
NM_001271282.2:c.3019C>T
NM_001291628.1:c.3019C>T
NM_030621.4:c.3019C>T
NM_001271282.3:c.3019C>T
NM_001291628.2:c.3019C>T
NM_177438.3:c.3019C>T
NM_001395677.1:c.3019C>T
NM_001395678.1:c.3019C>T
NM_001395679.1:c.3019C>T
NM_001395680.1:c.3019C>T
NM_001395682.1:c.3019C>T
NM_001395683.1:c.3019C>T
NM_001395684.1:c.3019C>T
NM_001395685.1:c.3019C>T
NM_001395686.1:c.2737C>T
NM_001395687.1:c.2614C>T
NM_001395688.1:c.2614C>T
NM_001395689.1:c.2614C>T
NM_001395690.1:c.2614C>T
NM_001395691.1:c.2452C>T
NM_001395692.1:c.3019C>T
NM_001395693.1:c.3019C>T
NM_001395694.1:c.3019C>T
NM_001395695.1:c.3019C>T
NM_001395696.1:c.2614C>T
NM_001395697.1:c.1336C>T
NR_172715.1:n.3437C>T
NR_172716.1:n.3621C>T
NR_172717.1:n.3531C>T
NR_172718.1:n.3531C>T
NR_172719.1:n.3364C>T
NR_172720.1:n.3364C>T

Pathogenic

Met criteria codes 4

PVS1 PM2_Supporting PS4_Supporting PP4

Not Met criteria codes 14

BS1 BS4 BS3 BP4 BP2 PM6 PM1 PM5 PS1 PS2 PS3 BA1 PP1 PP3

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.3019C>T (p.Gln1007Ter) variant in DICER1 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 19/27 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 (PS4_Supporting; PMID: 30178239, 28323992, 25118636, NCI). In addition, at least one patient with this variant 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: 28323992). 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

PVS1	✔	Nonsense variant upstream of residue 1850; predicted to undergo NMD
PM2_Supporting	✔	Absent from gnomAD 2.1 (non-cancer) with >20x coverage in the region
PS4_Supporting	✔	This variant received a total of 1 phenotype points for 1 proband meeting DICER1 VCEP phenotype specificity scoring criteria (PS4_Supporting; PMID: 30178239, 28323992, 25118636, NCI).
PP4	✔	At least one patient with this variant 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: 28323992).

Not Met criteria codes

BS1	✖	
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
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

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
PS3	✖	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
PP1	✖	Two meioses. Insufficient to apply.
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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