

*Variant: NM\_177438.3(DICER1):c.4313A>G (p.Tyr1438Cys)*

Version: 1.1

CA390869397 [↗](#)

939082 (ClinVar) [↗](#)

**Gene:** DICER1 ([HGNC:23405](#))

**Condition:** DICER1-related tumor predisposition ([MONDO:0100216](#))

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** d99efc02-b33a-43ca-ab46-adbf89b1bb85

**Approved on:** 2026-02-24

**Published on:** 2026-03-23

### *HGVS expressions*

#### **NM\_177438.3:c.4313A>G**

NM\_177438.3(DICER1):c.4313A>G (p.Tyr1438Cys)

NC\_000014.9:g.95096607T>C

CM000676.2:g.95096607T>C

NC\_000014.8:g.95562944T>C

CM000676.1:g.95562944T>C

NC\_000014.7:g.94632697T>C

NG\_016311.1:g.65816A>G

ENST00000529720.2:c.4313A>G

ENST00000531162.7:c.4313A>G

ENST00000674628.2:c.4313A>G

ENST00000675540.2:c.\*963A>G

ENST00000696733.1:c.4313A>G

ENST00000696734.1:c.4313A>G

ENST00000696735.1:n.1300A>G

ENST00000696736.1:c.4313A>G

ENST00000696737.1:c.4313A>G

ENST00000696920.1:n.4576A>G

ENST00000696921.1:n.5419A>G

ENST00000696922.1:n.4722A>G

ENST00000696923.1:c.4313A>G

ENST00000696924.1:c.4313A>G

ENST00000696925.1:n.4722A>G

ENST00000343455.8:c.4313A>G

ENST00000393063.6:c.4313A>G

ENST00000526495.6:c.4313A>G

ENST00000532939.3:c.4313A>G

ENST00000556045.6:c.4313A>G

ENST00000675540.1:c.2058A>G

ENST00000675995.1:c.\*2629A>G

ENST00000343455.7:c.4313A>G

ENST00000393063.5:c.4313A>G

ENST00000526495.5:c.4313A>G

ENST00000527414.5:c.4313A>G

ENST00000532939.2:c.348A>G

ENST00000541352.5:c.4313A>G

ENST00000556045.5:c.1007A>G

NM\_001195573.1:c.4313A>G  
NM\_001271282.2:c.4313A>G  
NM\_001291628.1:c.4313A>G  
NM\_030621.4:c.4313A>G  
NM\_177438.2:c.4313A>G  
NM\_001271282.3:c.4313A>G  
NM\_001291628.2:c.4313A>G  
NM\_001395677.1:c.4313A>G  
NM\_001395678.1:c.4313A>G  
NM\_001395679.1:c.4313A>G  
NM\_001395680.1:c.4313A>G  
NM\_001395682.1:c.4313A>G  
NM\_001395683.1:c.4313A>G  
NM\_001395684.1:c.4313A>G  
NM\_001395685.1:c.4313A>G  
NM\_001395686.1:c.4031A>G  
NM\_001395687.1:c.3908A>G  
NM\_001395688.1:c.3908A>G  
NM\_001395689.1:c.3908A>G  
NM\_001395690.1:c.3908A>G  
NM\_001395691.1:c.3746A>G  
NM\_001395692.1:c.4313A>G  
NM\_001395693.1:c.4313A>G  
NM\_001395694.1:c.4313A>G  
NM\_001395695.1:c.4313A>G  
NM\_001395696.1:c.3908A>G  
NM\_001395697.1:c.2630A>G  
NR\_172715.1:n.4731A>G  
NR\_172716.1:n.4915A>G  
NR\_172717.1:n.4825A>G  
NR\_172718.1:n.4748A>G  
NR\_172719.1:n.4581A>G  
NR\_172720.1:n.4658A>G

Uncertain Significance

Met criteria codes **2**

BP4 PM2\_Supporting

Not Met criteria codes **18**

BS2 PVS1 BS1 BS4 BS3  
BP7 BP2 PM1 PM5 PM4  
PS1 PS2 PS3 PS4 BA1 PP1  
PP3 PP4

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 1.4.0*

[Criteria Specification Approval History](#)





[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel



***DICER1 and miRNA-Processing Gene VCEP***























The NM\_177438.3:c.4313A>G variant in DICER1 is a missense variant predicted to cause substitution of tyrosine by cysteine at amino acid 1438 (p.Tyr1438Cys). Although this variant has been observed in individuals undergoing genetic sequencing, to our knowledge, this variant has not been reported in individuals with DICER1-related tumor predisposition (PS4 not met; Internal lab contributors). This variant has an allele frequency of 0.000001241 (2/1611784 alleles) across gnomAD v4.1.0 with no more than one allele in any subpopulation, which is lower than the ClinGen DICER1 VCEP threshold (<0.000005) for PM2\_Supporting, and therefore meets this criterion (PM2\_Supporting). In silico tools predict no damaging impact of the variant on protein function (REVEL: 0.2; MaxEntScan and SpliceAI: no effect on splicing) (BP4). 4 different missense variants, c.4313A>T (p.Tyr1438Phe), c.4313A>C (p.Tyr1438Ser), c.4312T>G (p.Tyr1438Asp), c.4312T>A (p.Tyr1438Asn), with Grantham scores equal to or less than the current variant have been reported in the same codon (ClinVar Variation ID: 2674813, 966537, 939902, 242107). However, these variants have not yet met the criteria to be classified as pathogenic by the ClinGen DICER VCEP (PM5 not met). In summary, this variant meets the criteria to be classified as Uncertain Significance for DICER1-related tumor predisposition based on the ACMG/AMP criteria applied, as specified by the ClinGen DICER1 VCEP: PM2\_Supporting, BP4. (Bayesian Points: 0; VCEP specifications version 1.4.0; 02/24/2026)

#### Met criteria codes

<b>BP4</b>			In silico tools predict no damaging impact of the variant on protein function (REVEL: 0.2; MaxEntScan and SpliceAI: no effect on splicing) (BP4).
<b>PM2_Supporting</b>			This variant has an allele frequency of 0.000001241 (2/1611784 alleles) across gnomAD v4.1.0 with no more than one allele in any subpopulation, which is lower than the ClinGen DICER1 VCEP threshold (<0.000005) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

#### Not Met criteria codes

<b>BS2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PVS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BS3</b>			Axent-Saipovski Thesis, 2024, McGill University: Development of a miRNA-based reporter assay. Variant looked like WT. See Fig 12 ( <a href="https://escholarship.mcgill.ca/concern/theses/mw22vc17n">https://escholarship.mcgill.ca/concern/theses/mw22vc17n</a> )
<b>BP7</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>BP2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

<b>PM1</b>			This variant does not reside within a region of the RNase IIIb domain that is defined as a critical functional domain by the ClinGen DICER1 VCEP (PM1 not met).
<b>PM5</b>			4 different missense variants, c.4313A>T (p.Tyr1438Phe), c.4313A>C (p.Tyr1438Ser), c.4312T>G (p.Tyr1438Asp), c.4312T>A (p.Tyr1438Asn), with Grantham scores equal to or less than the current variant have been reported in the same codon (ClinVar Variation ID: 2674813, 966537, 939902, 242107). However, these variants have not yet met the criteria to be classified as pathogenic by the ClinGen DICER VCEP (PM5 not met).
<b>PM4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS2</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS3</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PS4</b>			Although this variant has been observed in individuals undergoing genetic sequencing, to our knowledge, this variant has not been reported in individuals with DICER1-related tumor predisposition (PS4 not met; Internal lab contributors).
<b>BA1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PP1</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PP3</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
<b>PP4</b>			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History [↗](#)

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification ⓘ	Condition	Published Date	Version ⓘ	Criteria Specification	Gene
<a href="#">View</a>	NM_177438.3(DICER1):c.4313A>G (p.T...	<b>Uncertain Significance</b>	DICER1-Related Tumor Predisposition <a href="#">↗</a>	2026-03-23	1.1	ClinGen DICER1 and miRNA-Processing Gene Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for DICER1 Version 1.4.0 <a href="#">↗</a>	DICER1 <a href="#">↗</a>
<a href="#">View</a>	NM_177438.3(DICER1):c.4313A>G (p.T...	<b>Uncertain Significance</b>	DICER1-Related Tumor Predisposition <a href="#">↗</a>	2024-01-17	1.0	ClinGen DICER1 and miRNA-Processing Gene Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for DICER1 Version 1.2.0 <a href="#">↗</a>	DICER1 <a href="#">↗</a>

Showing 1 to 2 of 2 rows

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