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_000051.4(ATM):c.67C>T (p.Arg23Ter)

Version: 1.0

CA6264503

232248 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 69888cb6-ef49-4d1f-8999-03e7aefcf116
Approved on: 2024/11/26
Published on: 2025/1/13

HGVS expressions

NM_000051.4:c.67C>T
NM_000051.4(ATM):c.67C>T (p.Arg23Ter)
NC_000011.10:g.108227691C>T
CM000673.2:g.108227691C>T
NC_000011.9:g.108098418C>T
CM000673.1:g.108098418C>T
NC_000011.8:g.107603628C>T
NG_009830.1:g.9860C>T
ENST00000452508.7:c.67C>T
ENST00000683914.2:c.67C>T
ENST00000713593.1:c.67C>T
ENST00000278616.9:c.67C>T
ENST00000682147.1:n.201C>T
ENST00000682430.1:n.166C>T
ENST00000682465.1:c.67C>T
ENST00000682516.1:n.201C>T
ENST00000682956.1:n.201C>T
ENST00000683150.1:c.67C>T
ENST00000683174.1:n.217C>T
ENST00000683468.1:c.67C>T
ENST00000683488.1:n.4648C>T
ENST00000683914.1:c.67C>T
ENST00000684029.1:c.67C>T
ENST00000684037.1:c.67C>T
ENST00000684061.1:n.201C>T
ENST00000684179.1:n.201C>T
ENST00000527805.6:c.67C>T
ENST00000638443.1:c.67C>T
ENST00000639240.1:c.67C>T
ENST00000639953.1:c.67C>T
ENST00000640388.1:c.67C>T
ENST00000675595.1:c.67C>T
ENST00000675843.1:c.67C>T
ENST00000278616.8:c.67C>T
ENST00000452508.6:c.67C>T
ENST00000526567.5:c.67C>T
ENST00000527805.5:c.67C>T

ENST00000527891.5:c.67C>T
ENST00000530958.5:c.67C>T
ENST00000532931.5:c.67C>T
ENST00000601453.2:c.67C>T
NM_000051.3:c.67C>T
NM_001351834.1:c.67C>T
NM_001351835.1:c.67C>T
NM_001351836.1:c.67C>T
NM_001351834.2:c.67C>T
NM_001351835.2:c.67C>T
NM_001351836.2:c.67C>T

Pathogenic

Met criteria codes 3

PVS1 PM5 PM3_Strong

Not Met criteria codes 1

PM2

Evidence Links 0

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.3.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.67C>T (p.Arg23*) variant in ATM is a nonsense variant in a biologically-relevant-exon predicted to cause a premature stop codon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism. This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious. This variant has been detected in 4 at least individuals with Ataxia-Telangiectasia (PMID: 26896183, 35260754, 36439585). The highest population minor allele frequency in gnomAD v2.1.1 is 0.000098 in the South Asian population (PM2_Supporting, BS1, and BA1 are not met). In summary, this variant meets criteria to be classified as pathogenic for autosomal dominant ATM-related cancer predisposition and autosomal recessive Ataxia-Telangiectasia based on the ACMG/AMP criteria applied as specified by the HBOP Variant Curation Expert Panel. (PVS1, PM5_Supporting, PM3_Strong)

Met criteria codes

PVS1	✔	This variant in ATM is a nonsense variant predicted to cause a premature stop codon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM5	✔	This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (p.Arg3047*)
PM3_Strong	✔	This variant has been detected in atleast 4 individuals with Ataxia-Telangiectasia(PMID;36439585,26896183, 35260754)

Not Met criteria codes

PM2	✖	The variant has an allele frequency of 0.01% in the South asian population in gnomAD v2.1.1 which is higher than the threshold defined by HBOP VCEP(PM2_Supporting, BS1, and BA1 are not met)

Curation History

Showing 1 to 1 of 1 rows

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