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.8266A>T (p.Lys2756Ter)

Version: 1.0

CA293899

135780 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: f10fefda-685a-4bf8-8cab-190122d8c62b
Approved on: 2024/11/26
Published on: 2025/1/13

HGVS expressions

NM_000051.4:c.8266A>T
NM_000051.4(ATM):c.8266A>T (p.Lys2756Ter)
NC_000011.10:g.108335959A>T
CM000673.2:g.108335959A>T
NC_000011.9:g.108206686A>T
CM000673.1:g.108206686A>T
NC_000011.8:g.107711896A>T
NG_009830.1:g.118128A>T
NG_054724.1:g.138874T>A
ENST00000452508.7:c.8266A>T
ENST00000713593.1:c.*7737A>T
ENST00000278616.9:c.8266A>T
ENST00000525056.2:n.2685A>T
ENST00000638786.2:n.964A>T
ENST00000682286.1:n.3023A>T
ENST00000682302.1:n.2684A>T
ENST00000683174.1:n.9750A>T
ENST00000683524.1:n.3490A>T
ENST00000684152.1:n.3682A>T
ENST00000684180.1:n.740A>T
ENST00000684447.1:n.4759A>T
ENST00000527805.6:c.*3330A>T
ENST00000675595.1:c.*3401A>T
ENST00000675843.1:c.8266A>T
ENST00000278616.8:c.8266A>T
ENST00000452508.6:c.8266A>T
ENST00000524755.5:c.227-667T>A
ENST00000524792.5:n.4481A>T
ENST00000525056.1:n.463A>T
ENST00000525729.5:c.641-26888T>A
ENST00000527531.5:c.*1197-667T>A
ENST00000533979.5:n.478A>T
ENST00000615746.4:c.*1197-667T>A
NM_000051.3:c.8266A>T
NM_001330368.1:c.641-26888T>A
NM_001351110.1:c.695-667T>A
NM_001351834.1:c.8266A>T

NR_147053.2:n.2302-667T>A
NM_001330368.2:c.641-26888T>A
NM_001351110.2:c.695-667T>A
NM_001351834.2:c.8266A>T
NR_147053.3:n.2300-667T>A

Pathogenic

Met criteria codes 3

PVS1 PM5_Supporting 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.8266A>T (p.Lys2756*) variant in ATM is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 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-terminal pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious. This variant has been detected in at least 3 individuals with Ataxia-Telangiectasia (PMID: 10330348, 12552559, 26896183). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00003887 in the European (non-Finnish) population (PM2_Supporting, BS1, and BA1 are not met). In summary, this variant meets the 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 VCEP. (PVS1, PM5_Supporting, PM3_Strong)

Met criteria codes

PVS1	✔	The c.8266A>T (p.Lys2756*) variant in ATM is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminal pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious.
PM3_Strong	✔	This variant has been detected in at least 3 individuals with Ataxia-Telangiectasia (PMID: 10330348, 12552559, 26896183). 2 POINTS: one AT patient with second pathogenic variant (c.7010_7011del (p.Cys2337fs), Phenotype Confident, phase unknown. 2 POINTS: one AT patient with second pathogenic variant (c.2250G>A (p.Lys750=), Phenotype Confident, phase unknown. 2 POINTS: one AT patient with second pathogenic variant (c.1396C>T (p.Gln466Ter), Phenotype Confident, phase unknown. TOTAL=6pts

Not Met criteria codes

PM2	✖	The highest minor allele frequency in gnomAD v2.1.1 is 0.00003887 (5/128650 alleles) in European(non-Finnish) population (PM2_Supporting not met).

Curation History

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