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.4318A>T (p.Lys1440Ter)

Version: 1.0

CA16613046

407482 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: fb2bfa34-3766-4354-b984-640d17b7d239
Approved on: 2024/11/26
Published on: 2025/1/13

HGVS expressions

NM_000051.4(ATM):c.4318A>T (p.Lys1440Ter)
NM_000051.4:c.4318A>T
NC_000011.10:g.108289683A>T
CM000673.2:g.108289683A>T
NC_000011.9:g.108160410A>T
CM000673.1:g.108160410A>T
NC_000011.8:g.107665620A>T
NG_009830.1:g.71852A>T
ENST00000452508.7:c.4318A>T
ENST00000713593.1:c.*3789A>T
ENST00000278616.9:c.4318A>T
ENST00000533733.6:n.1581A>T
ENST00000683174.1:n.4468A>T
ENST00000527805.6:c.4318A>T
ENST00000675595.1:c.4153A>T
ENST00000675843.1:c.4318A>T
ENST00000278616.8:c.4318A>T
ENST00000452508.6:c.4318A>T
ENST00000524792.5:n.533A>T
ENST00000531525.2:c.325A>T
ENST00000533733.5:n.747A>T
NM_000051.3:c.4318A>T
NM_001351834.1:c.4318A>T
NM_001351834.2:c.4318A>T

Pathogenic

Met criteria codes 4

PM3 PM2_Supporting PVS1 PM5_Supporting

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.4318A>T (p.Lys1440*) variant in ATM gene 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-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 at least one individual with Ataxia-Telangiectasia (PMID: 26896183). This variant is absent from gnomAD v2.1.1. 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 VCEP. (PVS1, PM5_Supporting, PM3, PM2_Supporting)

Met criteria codes

PM3	✔	The c.4318A>T (p.Lys1440Ter) variant has been detected in at least one individual with Ataxia-Telangiectasia (2 points: PMID: 26896183)
PM2_Supporting	✔	Absent from controls (or at extremely low frequency if recessive) in GnomAD (V 2.1.1)
PVS1	✔	The c.4318A>T (p. Lys1440Ter) variant in ATM gene is a nonsense variant observed to cause premature truncation of the protein in exon 28/63 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM5_Supporting	✔	The c.4318A>T (p.Lys1440Ter) variant 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 deleterious(PM5_Supporting).

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.