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.2T>C (p.Met1Thr)

Version: 2.0

CA197209

187275 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: af70c135-df1b-4c1e-becb-96e5c6882dd5
Approved on: 2022/3/16
Published on: 2025/9/15

HGVS expressions

NM_000051.4:c.2T>C
NM_000051.4(ATM):c.2T>C (p.Met1Thr)
NC_000011.10:g.108227626T>C
CM000673.2:g.108227626T>C
NC_000011.9:g.108098353T>C
CM000673.1:g.108098353T>C
NC_000011.8:g.107603563T>C
NG_009830.1:g.9795T>C
ENST00000452508.7:c.2T>C
ENST00000683914.2:c.2T>C
ENST00000713593.1:c.2T>C
ENST00000278616.9:c.2T>C
ENST00000682147.1:n.136T>C
ENST00000682430.1:n.101T>C
ENST00000682465.1:c.2T>C
ENST00000682516.1:n.136T>C
ENST00000682956.1:n.136T>C
ENST00000683150.1:c.2T>C
ENST00000683174.1:n.152T>C
ENST00000683468.1:c.2T>C
ENST00000683488.1:n.4583T>C
ENST00000683914.1:c.2T>C
ENST00000684029.1:c.2T>C
ENST00000684037.1:c.2T>C
ENST00000684061.1:n.136T>C
ENST00000684179.1:n.136T>C
ENST00000527805.6:c.2T>C
ENST00000638443.1:c.2T>C
ENST00000639240.1:c.2T>C
ENST00000639953.1:c.2T>C
ENST00000640388.1:c.2T>C
ENST00000675595.1:c.2T>C
ENST00000675843.1:c.2T>C
ENST00000278616.8:c.2T>C
ENST00000452508.6:c.2T>C
ENST00000526567.5:c.2T>C
ENST00000527805.5:c.2T>C

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

Pathogenic

Met criteria codes 3

PM3_Very Strong | PVS1 | PM2_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 1.1*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The ATM c.2T>C (p.M1?) variant impacts the initiation codon and is not expected to produce a fully functional protein (PVS1). This variant has been observed in a compound heterozygous state in multiple individuals with Ataxia-Telangiectasia (PMIDs: 22146522, 3054930, 12552559, PM3_VeryStrong). This alteration has an allele frequency below 0.001% in the European (non-Finnish) subpopulation in GnomAD (PM2_Supporting). In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the HBOP Variant Curation Expert Panel.

Met criteria codes

PM3_Very Strong	✔	This variant has been observed in a compound heterozygous state (presumed) in multiple individuals with biallelic disease (PM3_VeryStrong, PMIDs: 30549301, 12552559, 22146522).
PVS1	✔	The c.2T>C variant impacts the initiation codon which is known to disrupt protein function (PVS1)
PM2_Supporting	✔	GnomAD AF 0.0009% (EUR) is less than ATM PM2 threshold of 0.001%

Curation History

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