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.743G>T (p.Arg248Leu)

Version: 1.0

CA382529260

453684 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 43eede42-e605-4230-8714-622f958ef2b8
Approved on: 2025/11/11
Published on: 2026/4/10

HGVS expressions

NM_000051.4(ATM):c.743G>T (p.Arg248Leu)
NM_000051.4:c.743G>T
NC_000011.10:g.108244868G>T
CM000673.2:g.108244868G>T
NC_000011.9:g.108115595G>T
CM000673.1:g.108115595G>T
NC_000011.8:g.107620805G>T
NG_009830.1:g.27037G>T
ENST00000452508.7:c.743G>T
ENST00000713593.1:c.*214G>T
ENST00000278616.9:c.743G>T
ENST00000682430.1:n.842G>T
ENST00000682516.1:n.877G>T
ENST00000682956.1:n.877G>T
ENST00000683100.1:n.3090G>T
ENST00000683174.1:n.893G>T
ENST00000683605.1:n.238G>T
ENST00000684037.1:c.743G>T
ENST00000684061.1:n.877G>T
ENST00000684179.1:n.712G>T
ENST00000527805.6:c.743G>T
ENST00000675595.1:c.578G>T
ENST00000675843.1:c.743G>T
ENST00000278616.8:c.743G>T
ENST00000452508.6:c.743G>T
ENST00000527805.5:c.743G>T
NM_000051.3:c.743G>T
NM_001351834.1:c.743G>T
NM_001351834.2:c.743G>T

Likely Pathogenic

Met criteria codes 3

PM3_Strong | PM2_Supporting | PP3

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 1.4.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.743G>T variant in ATM is a missense variant predicted to cause substitution of arginine by leucine at amino acid 248 (p.Arg248Leu). This variant has been detected in at least two unrelated individuals with Ataxia-Telangiectasia (PMIDs: 24120321, 26896183, 30713931). The filtering allele frequency (the upper threshold of the 95% CI of 5/1179886) of the c.743G>T variant in ATM is 0.000001240 for European (non-Finnish) chromosomes by gnomAD v4.1.0, which is lower than the HBOP VCEP threshold (≤0.00001) for PM2_Supporting, and therefore meets this criterion. The computational predictor REVEL gives a score of 0.836, which is above the threshold of 0.7333, evidence that correlates with impact to ATM function. In summary, this variant meets the criteria to be classified as likely 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. (PM3_Strong, PM2_Supporting, PP3)

Met criteria codes

PM3_Strong	✔	This variant has been detected in 2 unrelated individuals with Ataxia-Telangiectasia (PMID: 26896183, 30713931, 24120321, PM3_Strong).
PM2_Supporting	✔	The filtering allele frequency (the upper threshold of the 95% CI of 5/1179886) of the c.743G>T variant in ATM is 0.000001240 for European (non-Finnish) chromosomes by gnomAD v4.1.0, which is lower than the HBOP VCEP threshold (≤0.00001) for PM2_Supporting, and therefore meets this criterion.
PP3	✔	The computational predictor REVEL gives a score of 0.836, which is above the threshold of 0.733, evidence that correlates with impact to ATM function (PP3).

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.