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.8494C>T (p.Arg2832Cys)

Version: 2.0

CA287019

127459 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: a1f4fda0-ab77-4c22-a6be-6dc2f95f8e60
Approved on: 2024/1/25
Published on: 2025/9/15

HGVS expressions

NM_000051.4(ATM):c.8494C>T (p.Arg2832Cys)
NM_000051.4:c.8494C>T
NC_000011.10:g.108345818C>T
CM000673.2:g.108345818C>T
NC_000011.9:g.108216545C>T
CM000673.1:g.108216545C>T
NC_000011.8:g.107721755C>T
NG_009830.1:g.127987C>T
NG_054724.1:g.129015G>A
ENST00000452508.7:c.8494C>T
ENST00000713593.1:c.*7965C>T
ENST00000278616.9:c.8494C>T
ENST00000638786.2:n.1192C>T
ENST00000682286.1:n.3251C>T
ENST00000682302.1:n.2912C>T
ENST00000683174.1:n.9978C>T
ENST00000683524.1:n.3718C>T
ENST00000684152.1:n.3910C>T
ENST00000684180.1:n.968C>T
ENST00000684447.1:n.4987C>T
ENST00000527805.6:c.*3558C>T
ENST00000675595.1:c.*3629C>T
ENST00000675843.1:c.8494C>T
ENST00000278616.8:c.8494C>T
ENST00000452508.6:c.8494C>T
ENST00000524755.5:c.227-10526G>A
ENST00000524792.5:n.4709C>T
ENST00000525729.5:c.641-36747G>A
ENST00000526725.1:n.272-5454G>A
ENST00000527531.5:c.*1196+9097G>A
ENST00000615746.4:c.*1196+9097G>A
NM_000051.3:c.8494C>T
NM_001330368.1:c.641-36747G>A
NM_001351110.1:c.695-10526G>A
NM_001351834.1:c.8494C>T
NR_147053.2:n.2301+9097G>A
NM_001330368.2:c.641-36747G>A

NM_001351110.2:c.695-10526G>A
NM_001351834.2:c.8494C>T
NR_147053.3:n.2299+9097G>A

Likely Pathogenic

Met criteria codes 3

PP3 PM3_Strong PS3_Supporting

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 1.2.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.8494C>T variant in ATM is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 2832 (p.Arg2832Cys). This variant has been detected in at least 3 individuals with Ataxia-Telangiectasia (PMID: 26896183, 22017321, 26846839). The highest minor allele frequency in gnomAD v2.1.1 of 0.01% (2/16244 alleles) in the African/African American population (PM2_Supporting, BS1, and BA1 are not met). The computational predictor, Revel (Score: 0.83), predicts a damaging effect on ATM function. Additionally, experimental studies showed that this variant has impact on ATM kinase activity and protein levels but radiosensitivity was found to be intermediate compared to wild type (PMID: 18634022). In summary, this variant meets criteria to be classified as likely pathogenic for autosomal dominant hereditary breast cancer and autosomal recessive Ataxia-Telangiectasia based on the ACMG/AMP criteria applied, as specified by the HBOP VCEP. (PM3_Strong, PP3, PS3_supporting)

Met criteria codes

PP3	✔	REVEL predicted the score of 0.83 which is above thresholds defined by the HBOP VCEP for PP3
PM3_Strong	✔	This variant has been detected in atleast 3 individuals with Ataxia-Telangiectasia.(PMID: 26896183, 22017321, 26846839)
PS3_Supporting	✔	Experimental studies showed that this variant has impact on ATM kinase activity and protein levels but radiosensitivity was found to be intermediate compared to wild type

Not Met criteria codes

PM2	✖	This variant has a minor allele frequency in gnomAD v2.1.1 of 0.01% (2/16244 alleles) in the African/African American population (PM2_Supporting, BS1, and BA1 are not met).

Curation History

Showing 1 to 2 of 2 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.