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Variant: NM_000051.4(ATM):c.8045C>G (p.Thr2682Ser)

Version: 1.1

CA382561906

644144 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: cf42b25c-cac5-48e0-b3ca-83407767b8bb
Approved on: 2026/6/19
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HGVS expressions

NM_000051.4:c.8045C>G
NM_000051.4(ATM):c.8045C>G (p.Thr2682Ser)
NC_000011.10:g.108335003C>G
CM000673.2:g.108335003C>G
NC_000011.9:g.108205730C>G
CM000673.1:g.108205730C>G
NC_000011.8:g.107710940C>G
NG_009830.1:g.117172C>G
NG_054724.1:g.139830G>C
ENST00000452508.7:c.8045C>G
ENST00000713593.1:c.*7516C>G
ENST00000278616.9:c.8045C>G
ENST00000525056.2:n.2464C>G
ENST00000638786.2:n.743C>G
ENST00000682286.1:n.2802C>G
ENST00000682302.1:n.2463C>G
ENST00000683174.1:n.9529C>G
ENST00000683524.1:n.3269C>G
ENST00000684152.1:n.3461C>G
ENST00000684180.1:n.519C>G
ENST00000684447.1:n.4538C>G
ENST00000527805.6:c.*3109C>G
ENST00000675595.1:c.*3180C>G
ENST00000675843.1:c.8045C>G
ENST00000278616.8:c.8045C>G
ENST00000452508.6:c.8045C>G
ENST00000524755.5:c.299+217G>C
ENST00000524792.5:n.4260C>G
ENST00000525056.1:n.242C>G
ENST00000525729.5:c.641-25932G>C
ENST00000527531.5:c.*1269+217G>C
ENST00000533979.5:n.257C>G
ENST00000615746.4:c.*1269+217G>C
NM_000051.3:c.8045C>G
NM_001330368.1:c.641-25932G>C
NM_001351110.1:c.*38+217G>C
NM_001351834.1:c.8045C>G

NR_147053.2:n.2374+217G>C
NM_001330368.2:c.641-25932G>C
NM_001351110.2:c.*38+217G>C
NM_001351834.2:c.8045C>G
NR_147053.3:n.2372+217G>C

Pathogenic

Met criteria codes 3

PM3_Supporting PVS1 PM2_Supporting

Not Met criteria codes 1

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.8045C>G variant in ATM is a missense variant predicted to cause substitution of threonine by serine at amino acid 2682 (p.Thr2682Ser). This variant has been detected in individual(s) with Ataxia-Telangiectasia (PMID: 12815592). The highest population minor allele frequency in gnomAD v4.1.0 is 0.0.00002229 (1/44868alleles) in East Asian population; while this is higher than the HBOP VCEP threshold (≤0.00001) for PM2_Supporting, it is present in only one allele, meeting this criterion. The computational splicing predictor SpliceAI gives a score of 0.97 for donor gain, predicting that the variant disrupts the donor splice site of ATM. RNA analysis demonstrated that this variant leads to partial skipping of exon 54, resulting in an in-frame deletion (removes amino acids 2681-2717) that is predicted to escape nonsense mediated decay but adversely impact the FATKIN domain (Ambry internal data). 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. (PM3_Supporting, PM2_Supporting, PVS1[RNA]).

Met criteria codes

PM3_Supporting	✔	PMID: 12815592 This variant has been observed in an individual(In the list of variants detected from Iberian population(18 Hispanic-American families) with ataxia telangiectasia (A-T Patients) in Trans (Phased confirmed) with another ATM variant c.8150A>C (called LP by VCEP). *Of note, a clerical error previously listed that this variant co-occurred with c.8150T>G.
PVS1	✔	This variant leads to partial skipping of exon 54 (Ambry internal data), PVS1 (RNA)
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.0 is 0.0.00002229 (1/44868alleles) in East Asian population; while this is higher than the HBOP VCEP threshold ([≤0.00001]) for PM2_Supporting, it is present in only one allele, meeting this criterion.

Not Met criteria codes

PP3	✖	Applying PVS1[RNA] The computational splicing predictor SpliceAI gives a score of 0.97 for donor gain, predicting that the variant disrupts the donor splice site of ATM.

Curation History

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