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.8395_8404del (p.Phe2799fs)

Version: 1.0

CA194225

186242 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: e90af0fd-26d7-4c79-a519-c1b3a2772f61
Approved on: 2024-11-26
Published on: 2025-01-13

HGVS expressions

NM_000051.4:c.8395_8404delTTTCAGTGCC
NM_000051.4:c.8395_8404del
NM_000051.4(ATM):c.8395_8404del (p.Phe2799fs)
NC_000011.10:g.108343348_108343357del
CM000673.2:g.108343348_108343357del
NC_000011.9:g.108214075_108214084del
CM000673.1:g.108214075_108214084del
NC_000011.8:g.107719285_107719294del
NG_009830.1:g.125517_125526del
NG_054724.1:g.131486_131495del
ENST00000452508.7:c.8395_8404del
ENST00000713593.1:c.*7866_*7875del
ENST00000278616.9:c.8395_8404del
ENST00000638786.2:n.1093_1102del
ENST00000682286.1:n.3152_3161del
ENST00000682302.1:n.2813_2822del
ENST00000683174.1:n.9879_9888del
ENST00000683524.1:n.3619_3628del
ENST00000684152.1:n.3811_3820del
ENST00000684180.1:n.869_878del
ENST00000684447.1:n.4888_4897del
ENST00000527805.6:c.*3459_*3468del
ENST00000675595.1:c.*3530_*3539del
ENST00000675843.1:c.8395_8404del
ENST00000278616.8:c.8395_8404del
ENST00000452508.6:c.8395_8404del
ENST00000524755.5:c.227-8055_227-8046del
ENST00000524792.5:n.4610_4619del
ENST00000525729.5:c.641-34276_641-34267del
ENST00000526725.1:n.272-2983_272-2974del
ENST00000527531.5:c.*1197-8055_*1197-8046del
ENST00000615746.4:c.*1197-8055_*1197-8046del
NM_000051.3:c.8395_8404del
NM_001330368.1:c.641-34276_641-34267del
NM_001351110.1:c.695-8055_695-8046del
NM_001351834.1:c.8395_8404del
NR_147053.2:n.2302-8055_2302-8046del

NM_001330368.2:c.641-34276_641-34267del
NM_001351110.2:c.695-8055_695-8046del
NM_001351834.2:c.8395_8404del
NR_147053.3:n.2300-8055_2300-8046del

Pathogenic

Met criteria codes 3

PM5_Supporting PVS1 PM3_Very Strong

Not Met criteria codes 3

BS1 PM2 BA1

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.8395_8404del (p.Phe2799Lysfs*4) variant in ATM is a frameshift variant in a biologically-relevant-exon predicted to cause a premature stop codon 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 7 individuals with Ataxia-Telangiectasia (PMID: 9792409, 9887333, 10817650, 12815592, 19147735, 21833744, 26896183). The highest population minor allele frequency in gnomAD v2.1.1 is 0.000026 in the European (non-Finnish) population (PM2_Supporting, BS1, and BA1 are not met). 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. (PVS1, PM5_supporting, PM3_Very Strong)

Met criteria codes

PM5_Supporting	✔	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.
PVS1	✔	The c.8395_8404del p.Phe2799LysfsTer4 variant in ATM is a frameshift variant in a biologically-relevant-exon predicted to cause a premature stop codon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM3_Very Strong	✔	This variant has been detected in at least 7 individuals with Ataxia-Telangiectasia (15 points, PMIDs 19147735, 21833744, 12815592, 10817650, 9887333, 9792409, 26896183: PM3_VeryStrong)

Not Met criteria codes

BS1	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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