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.824del (p.Ser274_Leu275insTer)

Version: 2.0

CA349767

220121 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1484b53f-94c3-4f9f-8f34-5092caaa64b1
Approved on: 2023/9/5
Published on: 2025/9/15

HGVS expressions

NM_000051.4:c.824del
NM_000051.4(ATM):c.824del (p.Ser274_Leu275insTer)
NC_000011.10:g.108244949del
CM000673.2:g.108244949del
NC_000011.9:g.108115676del
CM000673.1:g.108115676del
NC_000011.8:g.107620886del
NG_009830.1:g.27118del
ENST00000452508.7:c.824del
ENST00000713593.1:c.*295del
ENST00000278616.9:c.824del
ENST00000682430.1:n.923del
ENST00000682516.1:n.958del
ENST00000682956.1:n.958del
ENST00000683100.1:n.3171del
ENST00000683174.1:n.974del
ENST00000683605.1:n.319del
ENST00000684037.1:c.824del
ENST00000684061.1:n.958del
ENST00000684179.1:n.793del
ENST00000527805.6:c.824del
ENST00000675595.1:c.659del
ENST00000675843.1:c.824del
ENST00000278616.8:c.824del
ENST00000452508.6:c.824del
ENST00000527805.5:c.824del
NM_000051.3:c.824del
NM_001351834.1:c.824del
NM_001351834.2:c.824del

Pathogenic

Met criteria codes 3

PVS1 PM5_Supporting PM3_Very Strong

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Not Met criteria codes 3

BA1 PM2 BS1

Evidence Links 0

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 c.824del (p.Leu275Ter) variant in ATM is a frameshift variant predicted to cause a premature stop codon in a biologically-relevant-exon 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-terminal 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 5 individuals with Ataxia-Telangiectasia (PMID: 26896183, 21792198, 9463314, 9887333). The c.824del (p.Leu275Ter) variant in ATM has a minor allele frequency in gnomAD v2.1.1 of 0.000018 in the non-Finnish European population (PM2_Supporting, BS1, and BA1 are not met). In summary, this variant meets criteria to be classified as 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. (PVS1, PM5_Supporting, PM3_VeryStrong)

Met criteria codes

PVS1	✔	The c.824del (p.Leu275Ter) variant in ATM is a nonsense variant predicted to cause a premature stop codon in a biologically-relevant exon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminal pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious (PM5_Supporting).
PM3_Very Strong	✔	This variant has been detected in at least 5 individuals with Ataxia Telangiectasia. Of those individuals, 4 were compound heterozygous for the variant and another ATM variant and 2 of those were confirmed in trans by parental. 1 individual was homozygous for the variant (8 Points: PM3_VeryStrong; PMID 26896183, 21792198, 9463314, 9887333).

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2	✖	The c.824del (p.Leu275Ter) variant in ATM has a minor allele frequency in gnomAD v2.1.1 of 0.000018 in the non-Finnish European population (BA1, BS1, PM2_supporting not met).
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 2 of 2 rows

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