

*Variant: NM_000051.4(ATM):c.6404_6405insTT
(p.Leu2135_Arg2136insTer)*

Version: 1.0

CA350459 [↗](#)

220763 (ClinVar) [↗](#)

Gene: ATM ([HGNC:472](#))

Condition: ATM-related cancer predisposition ([MONDO:0700270](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: fd96663e-d98d-4547-a241-db095eb19bca

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HGVS expressions

NM_000051.4(ATM):c.6404_6405insTT (p.Leu2135_Arg2136insTer)

NM_000051.4:c.6404_6405insTT

NC_000011.10:g.108320010_108320011insTT

CM000673.2:g.108320010_108320011insTT

NC_000011.9:g.108190737_108190738insTT

CM000673.1:g.108190737_108190738insTT

NC_000011.8:g.107695947_107695948insTT

NG_009830.1:g.102179_102180insTT

NG_054724.1:g.154823_154824insAA

ENST00000452508.7:c.6404_6405insTT

ENST00000713593.1:c.*5875_*5876insTT

ENST00000278616.9:c.6404_6405insTT

ENST00000525056.2:n.823_824insTT

ENST00000682286.1:n.1161_1162insTT

ENST00000682302.1:n.822_823insTT

ENST00000683174.1:n.7888_7889insTT

ENST00000683524.1:n.1628_1629insTT

ENST00000684152.1:n.2118_2119insTT

ENST00000527805.6:c.*1468_*1469insTT

ENST00000675595.1:c.*1468_*1469insTT

ENST00000675843.1:c.6404_6405insTT

ENST00000278616.8:c.6404_6405insTT

ENST00000452508.6:c.6404_6405insTT

ENST00000524792.5:n.2619_2620insTT

ENST00000525729.5:c.641-10939_641-10938insAA

ENST00000533690.5:n.1808_1809insTT

NM_000051.3:c.6404_6405insTT

NM_001330368.1:c.641-10939_641-10938insAA

NM_001351110.1:c.*39-10939_*39-10938insAA

NM_001351834.1:c.6404_6405insTT

NM_001330368.2:c.641-10939_641-10938insAA

NM_001351110.2:c.*39-10939_*39-10938insAA

NM_001351834.2:c.6404_6405insTT

Pathogenic

Met criteria codes 3

PM3_Very StrongPVS1PM5_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 1.3.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.6404_6405insTT (p.Arg2136*) 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. 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 8 individuals with Ataxia-Telangiectasia (PMIDs: 8659541, 9463314, 21665257). The highest population minor allele frequency in gnomAD v4.1.0 is 0.00001357 (16/1178720 alleles) in 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_VeryStrong)

Met criteria codes

PM3_Very Strong

This variant has been detected in at least 8 individuals with Ataxia-Telangiectasia (PMID: 8659541, 9463314, 21665257).

PVS1

The c.6404_6405insTT (p.Arg2136*) 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.

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.

Not Met criteria codes

PM2

The highest population minor allele frequency in gnomAD v4.1.0 is 0.00001357 (16/1178720 alleles) in European (non-Finnish) population (PM2_Supporting, BS1, and BA1 are not met).

Curation History

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