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Variant: NM_000051.4(ATM):c.4158dup (p.Lys1387Ter)

Version: 1.0

CA2695214771

3148196 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 347e9855-bece-4a30-ade8-c2f88b27b0ef
Approved on: 2025/6/19
Published on: 2026/4/10

HGVS expressions

NM_000051.4(ATM):c.4158dup (p.Lys1387Ter)
NM_000051.4:c.4158dup
NC_000011.10:g.108289025dup
CM000673.2:g.108289025dup
NC_000011.9:g.108159752dup
CM000673.1:g.108159752dup
NC_000011.8:g.107664962dup
NG_009830.1:g.71194dup
ENST00000452508.7:c.4158dup
ENST00000713593.1:c.*3629dup
ENST00000278616.9:c.4158dup
ENST00000533733.6:n.1421dup
ENST00000683174.1:n.4308dup
ENST00000527805.6:c.4158dup
ENST00000675595.1:c.3993dup
ENST00000675843.1:c.4158dup
ENST00000278616.8:c.4158dup
ENST00000452508.6:c.4158dup
ENST00000524792.5:n.373dup
ENST00000531525.2:c.165dup
ENST00000533733.5:n.587dup
NM_000051.3:c.4158dup
NM_001351834.1:c.4158dup
NM_001351834.2:c.4158dup

Pathogenic

Met criteria codes 4

PM3_Strong | PM2_Supporting | PVS1 | PM5_Supporting

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.4158dup (p.Lys1387*) variant in ATM is a nonsense variant predicted to cause a premature stop codon in 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 two unrelated individuals with Ataxia-Telangiectasia (PMID: 26896183). The highest minor allele frequency in gnomAD v4.1.0 is 0.00003381 (1/29576 alleles) in the Ashkenazi Jewish 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. 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_Strong, PM2_Supporting)

Met criteria codes

PM3_Strong	✔	This variant has been detected in at least 2 unrelated individuals with Ataxia-Telangiectasia (PMID: 26896183).
PM2_Supporting	✔	The highest minor allele frequency in gnomAD v4.1.0 is 0.00003381 (1/29576 alleles) in Ashkenazi Jewish population, which is higher than the ClinGen HBOP VCEP threshold (>.001%, N=1) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PVS1	✔	The c.4158dup (p.Lys1387Ter) (NM_000051.4) variant in ATM is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon leading to nonsense mediated decay (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).

Curation History

Showing 1 to 1 of 1 rows

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