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.6212T>A (p.Leu2071Ter)

Version: 1.0

CA382551078

826252 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 0fee42f1-f85f-4de8-a9c5-eb741c97e4bd
Approved on: 2024/11/26
Published on: 2025/1/13

HGVS expressions

NM_000051.4(ATM):c.6212T>A (p.Leu2071Ter)
NM_000051.4:c.6212T>A
NC_000011.10:g.108317386T>A
CM000673.2:g.108317386T>A
NC_000011.9:g.108188113T>A
CM000673.1:g.108188113T>A
NC_000011.8:g.107693323T>A
NG_009830.1:g.99555T>A
NG_054724.1:g.157447A>T
ENST00000452508.7:c.6212T>A
ENST00000713593.1:c.*5683T>A
ENST00000278616.9:c.6212T>A
ENST00000525056.2:n.631T>A
ENST00000682286.1:n.969T>A
ENST00000682302.1:n.630T>A
ENST00000683174.1:n.7696T>A
ENST00000683524.1:n.1436T>A
ENST00000684152.1:n.1926T>A
ENST00000527805.6:c.*1276T>A
ENST00000675595.1:c.*1276T>A
ENST00000675843.1:c.6212T>A
ENST00000278616.8:c.6212T>A
ENST00000452508.6:c.6212T>A
ENST00000524792.5:n.2427T>A
ENST00000525729.5:c.641-8315A>T
ENST00000532765.1:n.529T>A
ENST00000533690.5:n.1616T>A
NM_000051.3:c.6212T>A
NM_001330368.1:c.641-8315A>T
NM_001351110.1:c.*39-8315A>T
NM_001351834.1:c.6212T>A
NM_001330368.2:c.641-8315A>T
NM_001351110.2:c.*39-8315A>T
NM_001351834.2:c.6212T>A

Pathogenic

Met criteria codes 4

PM3 PVS1 PM2_Supporting 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.6212T>A (p.Leu2071*) variant in ATM gene 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-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 one individual with Ataxia-Telangiectasia (PMID: 26896183). This variant is absent from gnomAD v2.1.1. In summary, this variant meets 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, PM2_Supporting)

Met criteria codes

PM3	✔	The c.6212T>A (p. Leu2071Ter) variant has been detected in one individual with Ataxia-Telangiectasia (2 points: PMID: 26896183)
PVS1	✔	The c.6212T>A(p. Leu2071Ter) variant in ATM gene is a nonsense variant observed to cause premature truncation of the protein in exon 43/63 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM2_Supporting	✔	Absent from controls
PM5_Supporting	✔	The c.6212T>A (p. Leu2071Ter) variant 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 deleterious(PM5_Supporting).

Curation History

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