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.8161G>A (p.Asp2721Asn)*

Version: 1.0

*CA382562473*

*1054111 (ClinVar)*

**Gene**: ATM (HGNC:472)
**Condition**: ATM-related cancer predisposition (MONDO:0700270)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 00607ef5-45d1-47af-8947-3ba6d6650812
**Approved on**: 2025/11/11
**Published on**: 2026/4/10

## *HGVS expressions*

**NM_000051.4(ATM):c.8161G>A (p.Asp2721Asn)**
**NM_000051.4:c.8161G>A**
NC_000011.10:g.108335854G>A
CM000673.2:g.108335854G>A
NC_000011.9:g.108206581G>A
CM000673.1:g.108206581G>A
NC_000011.8:g.107711791G>A
NG_009830.1:g.118023G>A
NG_054724.1:g.138979C>T
ENST00000452508.7:c.8161G>A
ENST00000713593.1:c.*7632G>A
ENST00000278616.9:c.8161G>A
ENST00000525056.2:n.2580G>A
ENST00000638786.2:n.859G>A
ENST00000682286.1:n.2918G>A
ENST00000682302.1:n.2579G>A
ENST00000683174.1:n.9645G>A
ENST00000683524.1:n.3385G>A
ENST00000684152.1:n.3577G>A
ENST00000684180.1:n.635G>A
ENST00000684447.1:n.4654G>A
ENST00000527805.6:c.*3225G>A
ENST00000675595.1:c.*3296G>A
ENST00000675843.1:c.8161G>A
ENST00000278616.8:c.8161G>A
ENST00000452508.6:c.8161G>A
ENST00000524755.5:c.227-562C>T
ENST00000524792.5:n.4376G>A
ENST00000525056.1:n.358G>A
ENST00000525729.5:c.641-26783C>T
ENST00000527531.5:c.*1197-562C>T
ENST00000533979.5:n.373G>A
ENST00000615746.4:c.*1197-562C>T
NM_000051.3:c.8161G>A
NM_001330368.1:c.641-26783C>T
NM_001351110.1:c.695-562C>T
NM_001351834.1:c.8161G>A

NR_147053.2:n.2302-562C>T
NM_001330368.2:c.641-26783C>T
NM_001351110.2:c.695-562C>T
NM_001351834.2:c.8161G>A
NR_147053.3:n.2300-562C>T

**Likely Pathogenic**

**Met criteria codes** 4

PM3_Strong PM2_Supporting PP1 PP3

**Not Met criteria codes** 22

PM1 PM5 PM4 PM6 BA1 BS1 BS4 BS3 BS2 BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4 PVS1 PP2 PP4

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 1.4.0*

**Criteria Specification Approval History**

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Hereditary Breast, Ovarian and Pancreatic Cancer VCEP***

**The c.8161G>A variant in ATM is a missense variant predicted to cause substitution of aspartic acid to asparagine at amino acid 2721 (p.Asp2721Asn). This variant has been detected in at least two unrelated individuals with Ataxia-Telangiectasia (PMID: 21665257, 25122203). The variant has been reported to segregate with Ataxia-Telangiectasia in two affected family members from one family (PMID: 25122203). This variant is absent from gnomAD v4.1.0. The computational predictor REVEL gives a score of 0.957, which is above the threshold of 0.7333, evidence that correlates with impact to ATM function. In summary, this variant meets the criteria to be classified as likely 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. (PM3_Strong, PP1, PP3, PM2_Supporting)**

**Met criteria codes**

| | | |
|---|---|---|
| **PM3_Strong** | ✔ | One patient with clinical diagnosis found with variant in PMID: 21665257 - second variant not specified. Therefore 1 point assigned. Two patients with A-T diagnosis (internal communication confirmed they are siblings) found with nonsense variant (c.7456C.T/p.R2486X), phase confirmed in PMID: 25122203. Assigned 4 points for one patient. Therefore 5 points in total = PM3_Strong |
| **PM2_Supporting** | ✔ | This variant is absent from gnomADv4. |
| **PP1** | ✔ | Two siblings with confirmed diagnosis of A-T and nonsense variant in trans. Parents are confirmed to be carriers (internal communication, PMID: 25122203). Meets PP1_met as 1 segregation event is present. |
| **PP3** | ✔ | The REVEL score is 0.957 which is above the threshold for pathogenicity. SpliceAI scores show a very low risk of an impact on splicing. |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM1** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM5** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM4** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM6** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BA1** | ✖ | This variant is absent from gnomADv4. |
| **BS1** | ✖ | This variant is absent from gnomADv4. |
| **BS4** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS3** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS2** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP5** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP7** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP4** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP3** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP1** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP2** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

| | | | |
|---|---|---|---|
| **PS1** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS2** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS3** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS4** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PVS1** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP2** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP4** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

## Curation History

Showing 1 to 1 of 1 rows

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