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.2508dup (p.Ser837fs)

Version: 1.0

CA6265054

646712 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 836339ea-0018-4861-90d6-2771e4d4c3f8
Approved on: 2024/11/26
Published on: 2025/1/13

HGVS expressions

NM_000051.4:c.2508dup
NM_000051.4(ATM):c.2508dup (p.Ser837fs)
NC_000011.10:g.108267212dup
CM000673.2:g.108267212dup
NC_000011.9:g.108137939dup
CM000673.1:g.108137939dup
NC_000011.8:g.107643149dup
NG_009830.1:g.49381dup
ENST00000452508.7:c.2508dup
ENST00000713593.1:c.*1979dup
ENST00000278616.9:c.2508dup
ENST00000682516.1:n.2642dup
ENST00000683174.1:n.2658dup
ENST00000683605.1:n.2003dup
ENST00000684037.1:c.*1443dup
ENST00000527805.6:c.2508dup
ENST00000675595.1:c.2343dup
ENST00000675843.1:c.2508dup
ENST00000278616.8:c.2508dup
ENST00000452508.6:c.2508dup
ENST00000527805.5:c.2508dup
NM_000051.3:c.2508dup
NM_001351834.1:c.2508dup
NM_001351834.2:c.2508dup

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.2508dup (p.Ser837Ilefs*5) variant in ATM is a frameshift 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 1 individual with Ataxia-Telangiectasia (PMID: 26896183). This variant is absent from gnomAD v.2.1.1. 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, PM2_Supporting)

Met criteria codes

PM3	✔	This variant has been detected in 1 individual with Ataxia-Telangiectasia (PMID: 26896183). 2 POINTS: Phenotype confident, phase unknown, w/ ATM c.2250G>A (Clinvar consensus VLP/P, not yet curated by VCEP).
PVS1	✔	The c.2508dup (Ser837IlefsTer5) (NM_000051.4) variant in ATM is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon leading to nonsense mediated decay (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v.2.1.1 (PM2_Supporting).
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

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