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Variant: NM_000051.4(ATM):c.875C>T (p.Pro292Leu)

Version: 2.0

CA6264689

229794 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 7768fece-c9d1-45e4-9a70-6a4206150648
Approved on: 2024/1/25
Published on: 2025/9/15

HGVS expressions

NM_000051.4:c.875C>T
NM_000051.4(ATM):c.875C>T (p.Pro292Leu)
NC_000011.10:g.108245000C>T
CM000673.2:g.108245000C>T
NC_000011.9:g.108115727C>T
CM000673.1:g.108115727C>T
NC_000011.8:g.107620937C>T
NG_009830.1:g.27169C>T
ENST00000452508.7:c.875C>T
ENST00000713593.1:c.*346C>T
ENST00000278616.9:c.875C>T
ENST00000682430.1:n.974C>T
ENST00000682516.1:n.1009C>T
ENST00000682956.1:n.1009C>T
ENST00000683100.1:n.3222C>T
ENST00000683174.1:n.1025C>T
ENST00000683605.1:n.370C>T
ENST00000684037.1:c.875C>T
ENST00000684061.1:n.1009C>T
ENST00000684179.1:n.844C>T
ENST00000527805.6:c.875C>T
ENST00000675595.1:c.710C>T
ENST00000675843.1:c.875C>T
ENST00000278616.8:c.875C>T
ENST00000452508.6:c.875C>T
ENST00000527805.5:c.875C>T
NM_000051.3:c.875C>T
NM_001351834.1:c.875C>T
NM_001351834.2:c.875C>T

Likely Pathogenic

Met criteria codes 3

PP3 PM3_Strong PS3_Moderate

Not Met criteria codes 1

PM2

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.2.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.875C>T variant in ATM is a missense variant predicted to cause substitution of proline by leucine at amino acid 292 (p.Pro292Leu). This variant has been detected in at least 3 individuals with Ataxia-Telangiectasia (PMID: 18634022, 30549301, 26896183). The highest population minor allele frequency in gnomAD v2.1.1 is 0.005% (1/19890 alleles) in the East Asian population (PM2_Supporting, BS1, and BA1 are not met). Experimental studies shows that this variant has impact on ATM kinase activity, protein levels and radiosensitivity was also found to be sensitive (RS<21%) when compared with wild type (PMID:18634022,19431188). The REVEL computational prediction analysis tool predicted a score of 0.752, which is above the threshold necessary to apply PP3. In summary, this variant meets criteria to be classified as likely pathogenic for autosomal dominant hereditary breast cancer and autosomal recessive Ataxia-Telangiectasia based on the ACMG/AMP criteria applied, as specified by the HBOP VCEP. (PM3_strong, PS3_Moderate, PP3)

Met criteria codes

PP3	✔	The REVEL computational prediction analysis tool predicted a score of 0.752, which is above the threshold necessary to apply PP3.
PM3_Strong	✔	This variant has been detected in atleast 3 individuals with Ataxia-Telangiectasia.
PS3_Moderate	✔	Experimental studies shows that this variant has impact on ATM kinase activity, protein levels and radiosensitivity was also found to be sensitive(RS<21%) when compared with wild type

Not Met criteria codes

PM2	✖	The variant has an allele frequency of 0.005% in the East asian population in gnomAD v2.1.1 which is higher than the threshold defined by HBOP VCEP

Curation History

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