

## Gene Section

### Mini Review

# ATM (ataxia telangiectasia mutated)

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Published in Atlas Database: November 2002

Online updated version : <http://AtlasGeneticsOncology.org/Genes/ATM123.html>

DOI: 10.4267/2042/37923

This article is an update of :

Uhrhammer N, Bay JO, Gatti RA. ATM (ataxia telangiectasia mutated). *Atlas Genet Cytogenet Oncol Haematol.* 1999;3(4):173-174.

Huret JL. ATM (ataxia telangiectasia mutated). *Atlas Genet Cytogenet Oncol Haematol.* 1998;2(3):77-78

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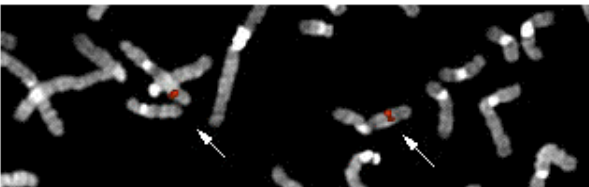
## Identity

**HGNC (Hugo):** ATM

**Location:** 11q22.3-q23.1

**Note:** See also, in Deep Insight section: Ataxia-Telangiectasia and variants.

## DNA/RNA



ATM (11q22.3) in normal cells: PAC 1053F10 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

## Description

66 exons spanning 184 kb of genomic DNA; numerous Alu and Lime sequences.

## Transcription

Alternative exons 1a and 1b; initiation codon lies within exon 4; 12 kb transcript with a 9.2 kb of coding sequence.

The ATM promoter is bi-directional and also directs the transcription of the E14/NPAT/CAND3 gene.

## Protein

### Description

3056 amino acids; 350 kDa; contains a PI 3-kinase-like domain (phosphatidylinositol 3-prime kinase).

## Expression

Found in all tissues.

## Localisation

Mostly in the nucleus throughout all stages of the cell cycle.

## Function

Initiates cell cycle checkpoints in response to double-strand DNA breaks by phosphorylating p53, BRCA1, H2AX, cAbl, I $\kappa$ B-alpha and chk1, as well as other targets; in certain types of tissues ATM inhibits radiation-induced, p53-dependent apoptosis.

## Homology

Phosphatidylinositol 3-kinase (PI3K)-like proteins, most closely related to ATR and the DNA-PK catalytic subunit.

## Mutations

### Germinal

Various types of mutations have been described, dispersed throughout the gene, and therefore most patients are compound heterozygotes; most mutations appear to inactivate the ATM protein by truncation, large deletions, or annulation of initiation or termination, although missense mutations have been described in the PI3 kinase domain and the leucine zipper motif.

Missense mutations outside of the PI3 kinase and leucine zipper domains have been described among breast cancer patients, although these mutations have not been found in A-T patients. Whether these mutations contribute to breast cancer though not to ataxia-telangiectasia remains controversial.

## Somatic

Biallelic mutation can occur in T-prolymphocytic leukaemia.

## Implicated in

### Ataxia telangiectasia

#### Disease

Ataxia telangiectasia is a progressive cerebellar degenerative disease with telangiectasia, immunodeficiency, cancer risk, radiosensitivity, and chromosomal instability.

#### Prognosis

Poor: median age at death: 17 yrs; survival rarely exceeds 30 yrs, though survival is increasing with improved medical care.

#### Cytogenetics

Spontaneous chromatid/chromosome breaks; non clonal stable chromosome rearrangements involving immunoglobulin superfamily genes e.g. inv(7)(p14q35); clonal rearrangements.

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*This article should be referenced as such:*

Uhrhammer N, Bay JO, Gatti RA. ATM (ataxia telangiectasia mutated). Atlas Genet Cytogenet Oncol Haematol. 2003; 7(1):12-13.

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