ATM (ataxia telangiectasia mutated)

Nancy Uhrhammer, Jacques-Olivier Bay, Richard A Gatti

Centre Jean-Perrin, BP 392, 63000 Clermont-Ferrand, France (NU, JOB, RAG)

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:

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2003 Atlas of Genetics and Cytogenetics in Oncology and Haematology

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 L1 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,cAbL1Kb-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.

References


This article should be referenced as such: