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Gene Section
Mini Review

ATM (ataxia telangiectasia mutated)

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Identity

Location : 11q22.3-q23.1

DNA/RNA

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

Protein

Description

3056 amino acids; 350 kDa; contains a Pl 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, cAbl, IkB-alpha and chk1, as well as other targets; in certain types of tissues ATM inhibits radiation-induced, p53-dependent apoptosis; a possible role in intercellular signaling has also been suggested.

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.

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 years; survival rarely exceeds 30 years, though survival is increasing with improved medical care.

Cytogenetics

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

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