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 LmI 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 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, cAbl, IkB-alpha and chkl, 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.

References


Greenwell PW, Kronmal SL, Porter SE, Gassenhuber J, Obermaier B, Petes TD. TEL1, a gene involved in controlling telomere length in S. cerevisiae, is homologous to the human ataxia telangiectasia gene. Cell. 1995 Sep 8;82(5):823-9


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