Ataxia-telengiectasia

GENERAL INFORMATION

Description:

Defects in ATM are the cause of ataxia talangiectasia, which includes four complementation groups: A, C, D and E. A-T is, complex, multysystem disorder.

Alternative names:

- AT
- AT1
- Louis-Bar syndrome
- Ataxia-telangiectasia (A-T) mutated

Classification:

- DNA breakage associated syndromes and DNA epigenetic modification syndromes
  - DNA-breakage-associated syndromes

Inheritance:

Autosomal recessive

OMIM:

- #208900 Ataxia-telangiectasia; AT
- *607585 Ataxia-telangiectasia; AT

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Nijmegen-breakage syndrome
- IDR factfile for Bloom syndrome

Incidence:

1: 100000 births.

CLINICAL INFORMATION

Description:

The disease is characterized by progressive cerebellar ataxia, dilation of the blood vessels in the conjunctiva and eyeballs, immunodeficiency, growth retardation and sexual immaturity. Patients have a strong predisposition to cancer; about 30% of patients develop tumors, particularly lymphomas and leukemias. Cells from affected individuals are highly sensitive to damage by ionizing radiation and resistant to inhibition of DNA synthesis following irradiation.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Ataxia telangiectasia, ORPHANET
- Ataxia telangiectasia, eMedicine

Genetic:

- SCDU Genetica Medica - Azienda Ospidaliera San Giovanni Battista di Torino, Italy, EDDNAL
- Ulleval University Hospital - Department of Medical Genetics (Oslo), Norway, EDDNAL
- Ulleval University Hospital - Department of Medical Genetics (Oslo), Norway, EDDNAL

Therapeutic options:

- Ataxia Telangiectasia, eMedicine

Research programs, clinical trials:

- Ataxia Telangiectasia Children's Project
- Ataxia Telangiectasia Children's Project
- European Initiative for Primary Immunodeficiencies
- Race for a cure, AT Children's project

GENE INFORMATION

Names:

HUGO name: ATM
Alias(es): AT, AT1, ATA, ATC, ATD, ATDC, T-PLL, TPLL, T-cell prolymphocytic leukemia, Serine-protein kinase ATM , EC 2.7.1.37

Localization:

Reference sequences:

DNA: U82828 (EMBL) U67092 (EMBL) U55757 (EMBL) U55757 (EMBL) , **cDNA:** U33841 (EMBL) U26455 (EMBL) X91196 (EMBL) , **Protein:** (SWISSPROT) Other Sequences

Chromosomal Location:

11q22-q23

Maps:

ATM (Map View)

Variations / Mutations:

- ATbase, Karolinska Insitutet, Sweden; ATbase, Karolinska Insitutet, Sweden
- Ataxia-Telangiectasia Mutation Database, Benaroya Research Institute, USA; Ataxia-Telangiectasia Mutation Database, Benaroya Research Institute, USA

Other gene-based resources:

Ensembl: ENSG00000149311, GENATLAS: ATM, GeneCard: ATM, UniGene: 435561, Entrez Gene: 472, euGenes: 472, GDB: 593364

PROTEIN INFORMATION

Description:

Protein function:

Involved in signal transduction, cell cycle control and DNA repair. May function as a tumor suppressor. Necessary for activation of abl1 and sapk. Phosphorylates p53, nfkbia, brca1, ctip, nibrin (nbs1), terf1, and rad9. May play a role in vesicle and/or protein transport. Inhibited by wortmaninn. Could play a role in T-cell development, gonad and neurological function.

Catalytic activity:

ATP + a protein = ADP + a phosphoprotein.

Subunit:

Exists in monomeric and tetrameric state. Binds DNA ends, p53, abl1, brca1, nibrin (nbs1) and terf1. Part of the brca1-associated genome surveillance complex (basc), which contains brca1, msh2, msh6, mlh1, atm, blm, pms2 and the rad50-mre11-nbs1 protein complex. This association could be a dynamic process changing throughout the cell cycle and within subnuclear domains.

Subcellular location:

Primarily nuclear. Found also in endocytic vesicles in association with beta-adaptin.

Post-translational modification:

Phosphorylated.

Induction:

By ionizing radiation.

Other features:

Other related resourses:

InterPro: IPR003151; FAT, InterPro: IPR003152; FATC, InterPro: IPR000403; PI3_PI4_kinase, Pfam: PF00454; PI3_PI4_kinase, Pfam: PF02259; FAT, Pfam: PF02260; FATC, SMART: SM00146; PI3Kc, SMART: SM00462; PTB, PROSITE: PS00915; PI3_4_KINASE_1, PROSITE: PS00916; PI3_4_KINASE_2, PROSITE: PS50290; PI3_4_KINASE_3

Expression pattern for human:

Tissue	Exp. (%)	Clones
CNS, multiple sclerosis lesions	7.76	3:7823
corresponding non cancerous liver tissue	7.28	5:13909
tonsil, enriched for germinal center B-cells	7.20	13:36522
aorta	5.91	3:10275
foveal and macular retina	5.00	1:4045
human optic nerve	4.59	1:4406
eye, retina	4.02	2:10065
uterus, pooled	3.91	3:15533
lung, 2 pooled	3.67	3:16549
neuroendocrine lung carcinoids		
adrenal gland	3.49	3:17391

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies

Disease specific:

- Ataxia-Telangiectasia, A-T Children's Project
- National Ataxia Foundation
- The Ataxia-Telangiectasia Medical Research Foundation
- National Ataxia Foundation to treat A-T
- The A-T project
- Ataxia Telangiectasia Research Foundation
- European Federation of hereditary ataxias