Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

GATA1 (GATA binding protein 1 (globin transcription factor1))

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Identity

Other names: ERYF1; GF1; NFE1

HGNC (Hugo): GATA1

Location: Xp11.23

Location (base pair): start at 48,401,210 bp from pter, ends at 48,408,967 bp from pter.

DNA/RNA

Description

Genomic sequence 7,757 bases, mRNA six exons (five coding) 1497bp. Plus strand.

Protein

Description

The full length GATA1 protein is 413 amino acids; 42.7 KDa. However two major protein isoforms are formed by alternative splicing of the mRNA and alternative translation initiation sites as shown in the figure. The shorter GATA1 protein (GATA1s) lacks the first 83 aa. ("The N-terminal activation domain AD"). GATA1s is less active in activation of megakaryocytic promoters. Both proteins contain two Zinc finger domains mediating protein interactions and DNA binding.

Expression

Bone-Marrow - Erythroid, Megakaryocytic, Mast and Eosonophillic precursors.

Localisation

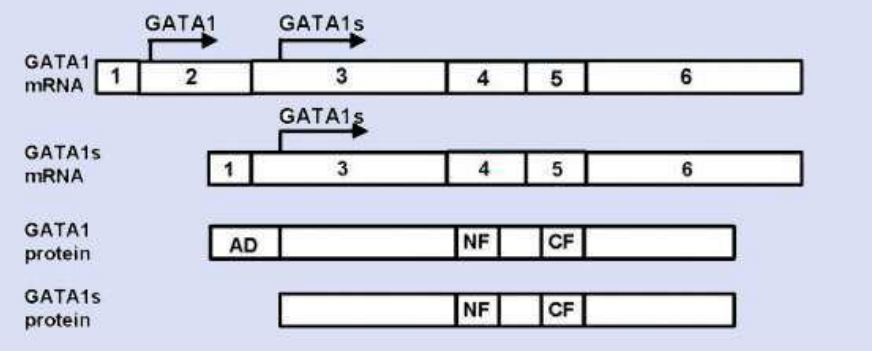
Nuclear

Function

Transcription Factor, essential for eryhtroid and megakaryocytic development.

Homology

A member of the family of GATA proteins.



Alternative models for generation of GATA1 isoforms. The full GATA1 protein can only be translated from the full GATA1 mRNA, whereas the GATA1s protein can be translated either from the full gata-1mRNA or from the shorter splice variant in which exon 2 is skipped.

Mutations

Germinal

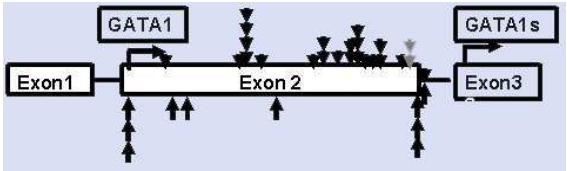
Implicated in germline mutations in the N- Zinc finger domain that mediates the interaction with FOG1 and/or binding to DNA, cause X-linked Dyserythropoietic anemia with thrombocytopenia. The syndrome can be also be manifested only by X-linked macrothrombocytopenia.

Somatic

See below.

Implicated in

Acquired somatic mutations in GATA1 occur in virtually all children with Down Syndrome (DS) and congenital transient myeloproliferative syndrome (TMD) or acute megakaryocytic leukemia (AMKL, M7-ANLL). The mutations have also been detected in umbilical cord blood of DS patients and in fetal liver of aborted DS embryos. The mutations occur in-utero probably during fetal liver hematopoiesis. They consist of insertions, deletions and base substitution in exon 2 and vicinity and all result in elimination of the full length GATA1 protein with preservation of the GATA1s isoform. The presence of GATA1s in the absence of full length GATA1 blocks megakaryocytic differentiation and promote proliferation of megakaryoblasts. The genes on chromosome 21 that promote this abnormality are unknown. GATA1 mutations are almost always associated with the M7 leukemia in DS although they were also described in a pair of twins with acquired trisomy 21 and in one adult non DS patient with M7. The down-regulations of genes regulated by GATA1 may explain the exquisite sensitivity of DS leukemic blasts to ACA-C.



Legend: Example to the distribution of the mutations in children with M7 and DS described in Rainis et al.

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