Leukaemia Section
Mini Review

del(11)(q23q23) MLL/ARHGEF12

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Disease
Acute myeloid leukemia (AML)

Epidemiology
Two cases so far: a 38-year-old male patient with a history of occupational exposure to herbicides and a M4-AML, and a 77-year-old female patient with a M5a-AML (Kourlas et al., 2000; Shih el al., 2006).

Evolution
The M4-AML patient underwent complete remission, but died 6 months later from an unrelated cause.

Cytogenetics

Cyto genetic morphological
The del(11)(q23q23) has been missed by cytogenetic analysis; both cases were hyperploid with +8 and other abnormalities.

Genes involved and proteins

MLL
Location
11q23.3
Protein
A major transcript of 14982 bp produces a 3969 amino acids protein from 36 of the 37 exons. Contains from N-term to C-term a binding site for MEN1, 3 AT hooks (binds to the minor groove of DNA); 2 speckled nuclear localisation signals; 2 repression domains RD1 and RD2: RD1 or CXXC; cystein methyl transferase, binds CpG rich DNA, has a transcriptional repression activity; RD2 recruits histone desacetylases HDAC1 and HDAC2; 3 plant homeodomains (cystein rich zinc finger domains, with homodimerization properties), 1 bromodomain (may bind acetylated histones), and 1 plant homeodomain; these domains may be involved in protein-protein interaction; a FYRN and a FRYC domain; a transactivation domain which binds CBP; may acetylates H3 and H4 in the HOX area; a SET domain: methyltransferase; methylates H3, including histones in the HOX area for allowing chromatin to be open to transcription. MLL is cleaved by taspase 1 into 2 proteins before entering the nucleus: a p300/320 N-term protein called MLL-N, and a p180 C-term protein, called MLL-C. The FYRN and a FRYC domains of native MLL associate MLL-N and MLL-C in a stable complex; they form a multiprotein complex with transcription factor TFIID. General transcription factor; maintains HOX genes expression in undifferentiated cells. Major regulator of hematopoiesis and embryonic development; role in cell cycle regulation.

ARHGEF12
Location
11q23.3
Protein
Better known as LARG, ARHGEF12 contains a PDZ (postsynaptic density protein, Drosophila disc large tumor suppressor, and zonula occludens-1 protein) domain, which localize ARHGEF12 to the membrane, a regulator of G protein signalling-like domain (RGSL or RH), which binds to activated heterotrimeric G protein alpha12/13 subunits, a Dbl homology (DH) domain, responsible for exchange activity, and a pleckstrin homology (PH) domain, involved in the regulation of the process. Regulatory protein involved in the GDP/GTP exchange reaction of the Rho proteins; activates a Rho-GTPase-dependent signaling pathway; activated by FYN.
Result of the chromosomal anomaly

**Hybrid gene**

**Description**

5' MLL - 3' ARHGEF12

**Fusion protein**

**Description**

Joins amino acid 1362 from MLL to amino acid 309 from ARHGEF12. The fusion protein comprises the Ala/Gly/Ser-rich region, poly-Gly stretch, three AT hooks domains, poly-Pro stretches, and Zinc finger CXXC-type domain from MLL fused to the RGSL, DH, PH domains of ARHGEF12.

**References**


This article should be referenced as such: