**Atlas of Genetics and Cytogenetics in Oncology and Haematology**

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# Leukaemia Section

## Mini Review

# t(2;11)(q37;q23) in AML

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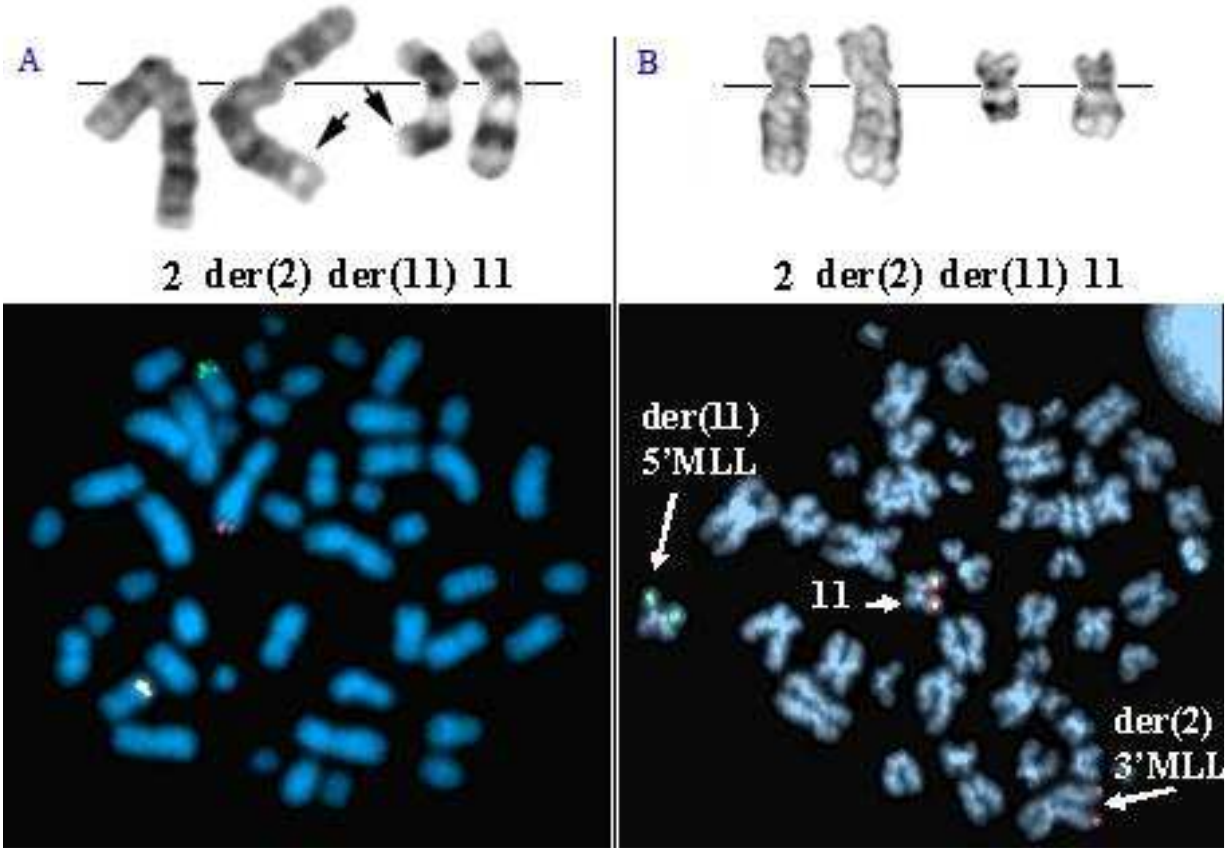
## Identity




t(2;11)(q37;q23) by G-banding and FISH with dual-color, break-apart MLL probe; Cecilia, Manuel R Teixeira (left); partial GTG-banded karyotype of t(2;11)(q37;23) and FISH analysis using probe LSI MLL DCBA demonstrating a 11q23 MLL rearrangement with a fusion signal on the normal chromosome 11, a split 5'MLL signal on der(11) and a 3'MLL signal on der(2); courtesy Arjan Buijs and Ellen van Binsbergen (right).

| Report | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| by | DeLozier-Blanchet | Winick | Fischer | Cerveira | van Binsbergen |
| Yr | 1985 | 1993 | 1997 | 2006 | 2007 |
| Disease | AML M5a | AML M4 | AML NOS | AML M4 | AML M2 |
| Age (Y)/gender | 76/F | 12.4/M | Adult/F | 54/F | 68/M |
| Pre CT/RT | no | yes | no | yes | yes |
| Karyotype | 46,XX,t(2;11) (q37;q23) | 46,XY,t(2;11) (q37;q23) | 46,XX,t(2;11) (q37;q23) | 46,XX,t(2;11) (q37;q23) | 46,XY,t(2;11) (q37;q23) |
| Additional | t(7;9;10) (q22;q22;p13) | | del(7)(q11) | | evolution 51,idem... |
| Survival (mo) | 9 | induction | NA | remission (after SCT) | 17 |

# Clinics and pathology

## Disease

Rare type of acute non lymphocytic leukemia (ANLL) and therapy-related ANLL.

## Phenotype / cell stem origin

No specific AML FAB sub-type (two cases M4, one M2, one M5a and one NOS).

## Etiology

Either de novo or therapy-related (prior cancer is variable: breast cancer, non-Hodgkin lymphoma and LLA).

## Epidemiology

Five cases known in the literature; four adults and one child, sex ratio 2M/3F; (age range 14.4-76).

## Prognosis

Two cases showed poor survival, 9 and 17 months respectively, one case achieved remission after stem cell transplantation. The prognosis may be likely to be comparable with that of other entities with 11q23/MLL involvement, and worse in therapy related leukemias.

# Genes involved and Proteins

## SEPT2

**Location:** 2q37
**DNA/RNA**

The SEPT2 gene has 14 exons.
SEPT2 has four types of transcripts with 3.6 kb, 3.5 kb, 3.4 kb and 3.3 kb encoding the same protein, as a result of alternative splicing.

**Protein**

SEPT2 belongs to an evolutionarily conserved family of genes that encode a P loop-based GTP-binding domain flanked by a polybasic domain and (usually) a coiled-coil region, and assemble into homo- and hetero-oligomers and filaments with key roles in cell division cytoskeletal dynamics and secretion. The SEPT2 gene codes for a protein with 361 amino acids and a molecular weight of 41.5 kDa.
SEPT2 was identified as a gene expressed in early embryonic mouse brain and down-regulated during development. It is ubiquitously expressed in cell lines and tissues with the highest protein levels found in brain tissue.
The SEPT2 protein, like other septin family members, is thought to be cytoplasmic. SEPT2 co-localises with actin filaments in interphase cells, and in dividing cells concentrates at the cleavage furrow.
SEPT2 is a multifunctional protein that was shown to be required for cytokinesis and to bind actin and associate with focal adhesions. Recent data support the idea that SEPT2 can have a role in chromosome congression and segregation. Additional functions have also been suggested; for instance, in rat brain lysates SEPT2 is part of a multi-septin complex that interacts with the exocyst complex, which plays a role in secretion and neurite outgrowth. SEPT2 has also been localised to senile plaques of brains in patients with Alzheimer's disease suggesting a role in neurodegeneration.
The SEPT2 protein belongs to an evolutionarily family of proteins with at least 14 members and shares a very high homology with septin 1, septin 4 and septin 5.

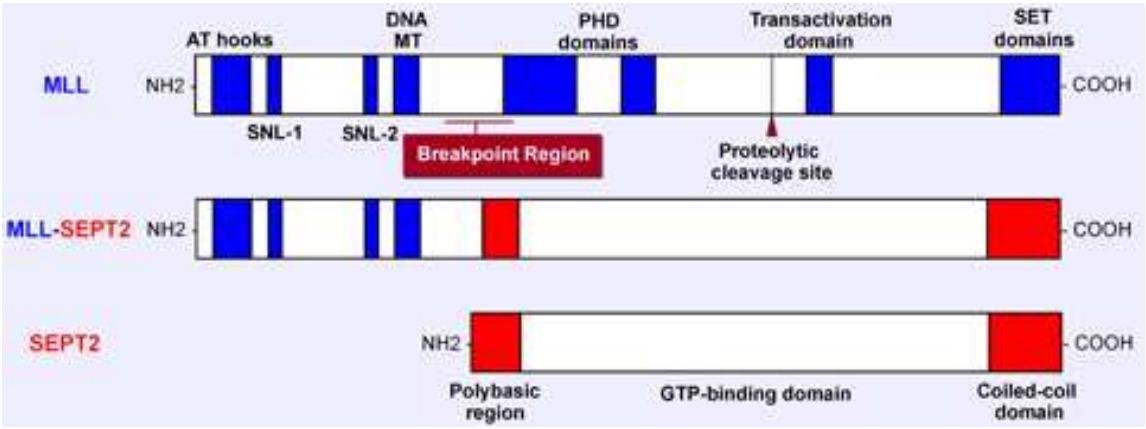
## MLL

**Location:** 11q23
**DNA/RNA**

37 exons, spanning over 100 kb.
In a centromeric to telomeric direction; 13 and 15 kb; coding sequence: 11.9 kb.

**Protein**

3969 amino acids; 431 kDa; contains from N-term to C-term 3 AT hooks homologous to high mobility group proteins HMGA1 and HMGA2, binding to the minor grove 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




Structure of the normal MLL and SEPT2 proteins and the resulting MLL-SEPT2 fusion protein.

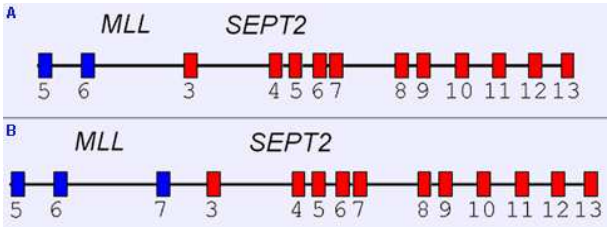
transcriptional repression activity; RD2 recruits histone desacetylases HDAC1 and HDAC2; 3 plant homeodomains (cystein rich zinc finger domains, with homodimerization properties), 1 bromodomain (may bind acetylated histones), and 1 plant homeodomain; these domains may be involved in protein-protein interaction; 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; methyltates 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.

# Results of the chromosomal anomaly

## *Hybrid gene*

**Description**

MLL-SEPT2. MLL exon 6 or 7 fused with SEPT2 exon 3.




## *Fusion protein*

**Description**

AT hook, SNL-1, SNL-2 and DNA methyltransferase domains from MLL fused to almost the entire open-reading frame of SEPT2, except for the first three aminoacids.

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*This article should be referenced as such:*

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