Atlas of Genetics and Cytogenetics
in Oncology and Haematology

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# Leukaemia Section
## Mini Review

# inv(11)(q21q23) in therapy related leukemias

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## Clinics and pathology

### Disease

Therapy-related acute leukemia and myelodysplastic syndromes (MDS).

### Phenotype / cell stem origin

M2-ANLL, acute monocytic leukemia, MDS, T-ALL.

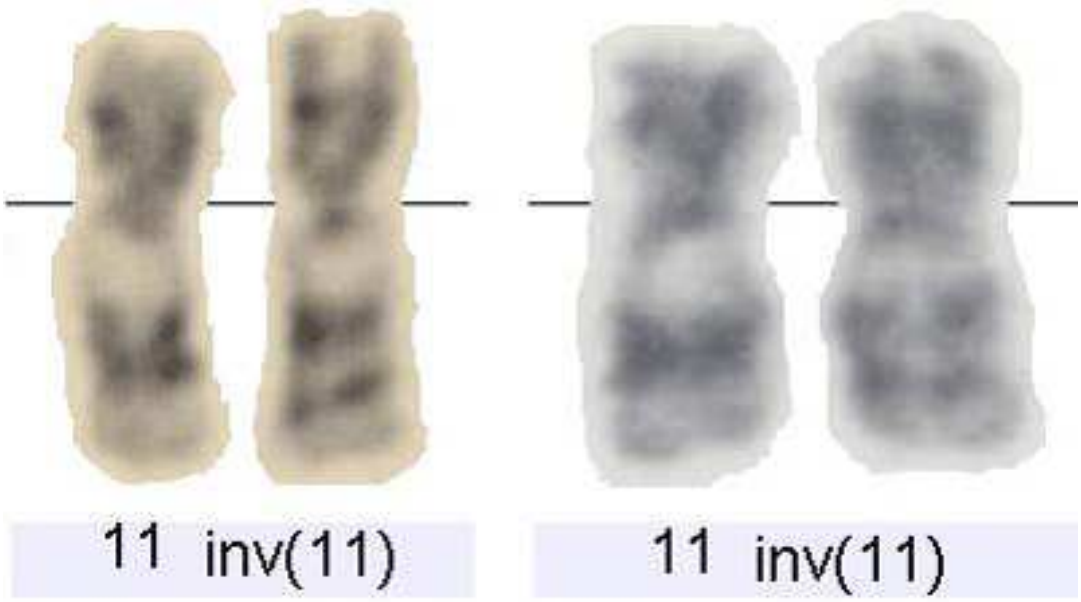
### Etiology

Latency from twenty months to six years after chemotherapy.

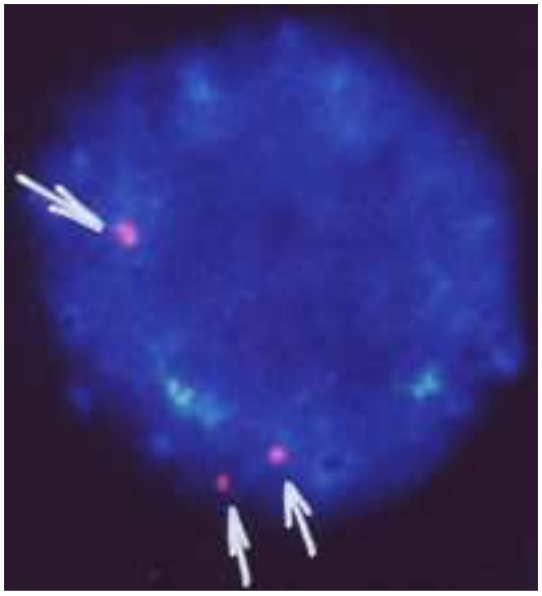
### Pathology

inv(11) positive cells were detectable six years prior to apparent leukemia in one case. MLL-MAML2 positive cells were detectable up to two years prior to apparent leukemia in another case. Whole genome expression profiles demonstrated differential expression of both typical MLL and NOTCH downstream genes.

## Cytogenetics




inv(11)(q21q23) G-banding.



Detection of MLL rearranged cell by fluorescence in situ hybridization (FISH) with an MLL split signal probe.

## Genes involved and Proteins

### *MAML2*

**Location:** 11q21

**DNA / RNA**

Spans 365 kb; 5 exons a major transcript of 7.5 kb.

**Protein**

1153 aa, 125 kDa; conserved N-terminal basic domain (aa 29-92) which binds to the ankyrin repeat domain of Notch receptors; two acidic domains (aa 263-360 and 1124-1153) and a C-terminal transcriptional activation domain.

### *MLL*

**Location:** 11q23

**DNA / RNA**

21 exons, spanning over 100 kb; 13-15 kb mRNA.

**Protein**

3969 amino acids; 431 kDa; contains two DNA binding motifs: a AT hook homologous to high mobility group proteins HMGI-(Y) and HMGI(C) that binds to the minor groove of DNA, and zinc fingers, a DNA methyl transferase motif, a bromodomain, and segments of homology with trithorax, in particular in the C-terminal SET domain.

## Results of the chromosomal anomaly

### *Hybrid gene*

**Description**

MLL-MAML2

**Transcript**

MLL-MAML2; exon 1-7 of MLL fused to exons 2-5 of MAML2.

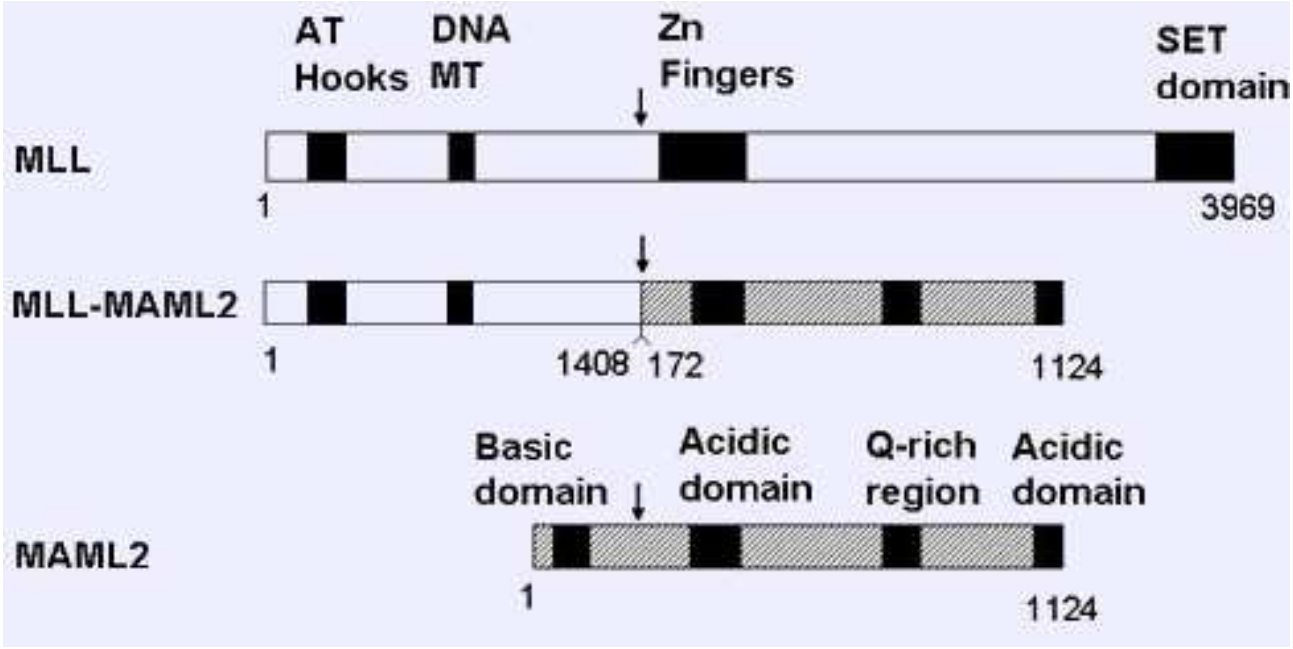
### *Fusion protein*

**Description**

Hybrid transcript MLL/MAML2 contains the following domains:
- from MLL: AT-hook, DNA-Methyltransferase;
- from MAML2: Q rich domain, acidic domain.

**Expression localisation**

In the nucleus.



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