

# Leukaemia Section

## Short Communication

### t(5;17)(q35;q21)

**Franck Vigié**

Laboratoire de Cytogénétique - Service d'Hématologie Biologique, Hôpital Hôtel-Dieu, 75181 Paris Cedex 04, France (FV)

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## Clinics and pathology

### Disease

Acute non lymphocytic leukemia (ANLL).

### Phenotype/cell stem origin

Acute promyelocytic leukemia (ANLL-M3 according to the FAB classification).

### Etiology

Exceptional; only 2 well documented cases.

### Clinics

Both patients were pediatric cases: F/2.5 years, M/12 years; disseminated intravascular coagulation at diagnosis in one case; remission obtained with chemotherapy and/or ATRA; first relapse at 7 and 5 months respectively.

### Cytology

Hypergranular and hypogranular bilobed promyelocytes; absence of Auer rods; typical microspeckled pattern with anti-RARa antibodies; terminal differentiation of blasts and promyelocytes in vitro with ATRA.

### Prognosis

Probably unfavorable (both patients had a short term first relapse).

## Cytogenetics

### Probes

RARa probe commercially available coupled with PML probe in dual color kits; non commercialized probes for NPM, previously used for t(2;5)(p23;q35) of anaplastic large cell lymphoma (same breakpoint into NPM) = cosmid clones 13, 15-2 and 47C12 retained by der(5).

### Additional anomalies

One of the two cases had complex additional abnormalities.

### Variants

t(15;17)(q22;q21) t(11;17)(q23;q21) t(11;17)(q13;q21)

## Genes involved and proteins

### NPM1

#### Location

5q35

#### Protein

Gene for the nucleolar phosphoprotein nucleophosmin; would participate in ribosome assembly.

### RARa

#### Location

17 q21

#### Protein

Gene for the retinoic acid receptor alpha; the breakpoint lies within the second intron of the gene, as in t(15;17) and t(11;17) translocations.

## Result of the chromosomal anomaly

### Hybrid gene

#### Description

Two reciprocal fusion genes are generated: 5'-NPM + 3'-RARa on der(5) and 5'-RARa + 3'-NPM on der(17); both fusion genes are transcribed, the crucial one is NPM-RARa; two NPM-RARa chimeric cDNAs are generated, one short and one long differing from 129 bp, with corresponding transcripts of 2.3 and 2.4 kb (alternatively spliced transcripts); in one case, only the

short NPM-RARa isoform could be detected; the 5' end of NPM-RARa cDNAs contains the first 442 bp of the NPM cDNA; the 3' end contains RARa sequences of exon 3 through the 3' end of RARa; a reciprocal RARa-NPM transcript is detected: RARa exons 1 and 2 are fused to 3' NPM downstream bp 443.

#### Detection

Nested RT-PCR.

#### Fusion protein

#### Description

Two NPM-RARa proteins, of 563 and 520 amino acids, are encoded (MW 62 and 57 kDa); NPM-RARa fusion protein acts as a retinoic acid-responsive transcriptional activator: increase of activity in a concentration dependant manner.

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