

# Leukaemia Section

## Short Communication

## t(3;21)(q26;q11) NRIP1/MECOM

Jean-Loup Huret

Medical Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France. jean-loup.huret@chu-poitiers.fr

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### Abstract

Review on t(3;21)(q26;q11), with data on clinics, and the genes involved.

#### Keywords

chromosome 3; chromosome 21; t(3;21)(q26;q11); MECOM; NRIP1

### Clinics and pathology

#### Note

Ten cases available, but with almost no data (Bobadilla et al., 2007; Haferlach et al., 2012).

#### Disease

#### Phenotype/cell stem origin

Out of ten cases, there were four acute myeloid leukemia (AML) cases, and six myelodysplastic syndromes (MDS)

#### Epidemiology

t(3;21)(q26;q11) represented about 1% of a cohort of 606 AML and 377 MDS patients with normal karyotypes (n = 594) or chromosome 7 alterations (-7/7q-; n = 389). Median age was 49 years (range 25-76) (Haferlach et al., 2012).

#### Clinics

Median WBC count was  $60.0 \times 10^9/L$  (range 2.4-15.0)

#### Cytogenetics

Cryptic rearrangement.

#### Prognosis

Survival outcomes in 22 patients with cryptic MECOM rearrangements (t(3;21)(q26;q11),

inv(3)(p24q26), and der(7)t(3;7)(q26;q21) altogether) and were compared with inv(3)(q21q26)/t(3;3)(q21;q26) cases.

Median overall survival was 9.4 months in the subgroup with cryptic MECOM rearrangements which was not significantly different from the 21.8 months in patients with an inv(3)(q21q26)/t(3;3)(q21;q26) (Haferlach et al., 2012).

### Genes involved and proteins

#### MECOM (Ecotropic Viral Integration Site 1 (EVI1) and Myelodysplastic Syndrome 1 (MDS1-EVI1))

#### Location

3q26.2

#### Note

MECOM is a nuclear transcription factor that plays an essential role in the proliferation and maintenance of hematopoietic stem cells and can inhibit myeloid differentiation.

Two alternative forms exist, one generated from EVI1, the other MECOM (MDS1 and EVI1 complex locus) through intergenic splicing with MDS1 (myelodysplasia syndrome 1), a gene located 140 kb upstream of EVI1.

#### Protein

The protein encoded by this gene is a transcriptional regulator involved in cell differentiation and proliferation, and apoptosis. The encoded protein can interact with transcriptional coactivators (P/CAF, CBP) and corepressors (CTBP1, HDAC) as

well as other transcription factors (GATA1, Smad3) (de Braekeleer et al., 2012)

### **NRIP1 (nuclear receptor interacting protein 1)**

#### **Location**

21q11.2

#### **Protein**

NRIP1 is a co-repressor of a large number of nuclear receptors. NRIP1 interacts preferentially with ligand-bound nuclear receptors and inhibits transactivation by recruitment of histone deacetylases and CtBP. NRIP1 interacts with ESR2 (Estrogen Receptor 2 (ER beta)) in ovarian cancer cells and ESR2 and E2F (in particular E2F1) transcription factors in breast cancer cells, represses their transcriptional activities and inhibits cell proliferation. NRIP1 increases APC expression exerting a negative control on the Wnt/  $\beta$ -catenin signaling in human colon cancer cells. Repression of CTNNB1 ( $\beta$ -catenin) by NRIP1 has also been described in hepatocellular carcinoma (Spinella, 2010; Lapierre et al., 2015).

## **Result of the chromosomal anomaly**

### **Hybrid gene**

#### **Description**

Breakpoints were located in introns 2 or 4 in EVI1,

and in introns 1, 2, or 3 in NRIP1 (Haferlach et al., 2012).

### **Fusion protein**

#### **Oncogenesis**

Increased MECOM expression was noted.

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