

# Leukaemia Section

## Short Communication

### t(7;11)(p15;p15) NUP98/HOXA13

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### Abstract

Several t(7;11)(p15;p15) have been reported in myeloid neoplasms. The most common is the one leading to a fusion between the NUP98 (11p15) and the HOXA9 (7p15).

A more rare t(7;11) is the one that leads to a fusion between the NUP98 and the HOXA13 gene on 7p15. This particular t(7;11) is associated primarily with acute myeloid leukemia (AML), primarily FAB M2 and M4. However, it has been reported also in one case of chronic myelogenous leukemia (CML) in blast crisis. The NUP98/HOXA13 fusion protein is thought to promote leukemogenesis through inhibition of HOXA13-mediated terminal differentiation and/or aberrant nucleocytoplasmic transport. . The protein encoded by the

NUP98/HOXA13 fusion gene is similar to the one encoded by the NUP98/HOXA9 fusion, and the expression pattern of the HOXA13 gene in leukemic cell lines is similar to that of the HOXA9 gene, suggesting that the NUP98/HOXA13 fusion protein may play a role in leukemogenesis through a mechanism similar to that of the NUP98/HOXA9 fusion protein.

### Keywords

chromosome 7; chromosome 11; t(7;11)(p15;p15); acute myeloid leukemia (AML); chronic myelogenous leukemia (CML); NUP98; HOXA13

### Identity

Precise breakpoints are the following: t(7;11)(p15.2;p15.4).



Figure 1 46,XX,t(7;11)(p15;p15)

## Clinics and pathology

### Note

This rare t(7;11) has been reported in: Acute myeloid leukemia (AML) Chronic myelogenous leukemia (CML) in blast crisis

### Disease: Acute myeloid leukemia (AML)

#### Phenotype/cell stem origin

The blasts expressed CD7, CD11b, CD13, CD33, CD34, and HLADR antigens.

### Clinics

De novo AML reported in a single patient, a 57 year-old woman (Taketani et al, 2002). The patient presented with leukocytosis (118,800/  $\mu$ L) and 81% myeloid blasts.

### Cytogenetics

At diagnosis, the karyotype was 46,XX,t(7;11)(p15;p15) in all 20 metaphase cells examined from a bone marrow sample. At remission, all 20 metaphase cells obtained from the bone marrow were normal, 46,XX. The t(7;11) seems to be a solitary abnormality in AML. No additional abnormalities have been reported so far.

### Treatment

Patient received induction therapy with idarubicin and cytarabine (AraC), followed by multiple cycles of AraC and anthracyclines.

### Evolution

A relapse occurred in the central nervous system 6 months after diagnosis and in the bone marrow 8 months after diagnosis, and the patient died of progressive disease 16 months after onset.

### Prognosis

The prognosis in this single case of AML is unfavorable.

### Disease: Chronic myelogenous leukemia (CML) in blast crisis

#### Epidemiology

This is the only described case so far of a CML in blast crisis presenting with a t(7;11)(p15;p15) in addition to the t(9;22)(q34;q11.2) (Di Giacomo et al., 2014).

### Clinics

The patient is a 39 year-old man referred for leukocytosis, mild anemia, thrombocytopenia, and splenomegaly. CML in blast crisis was diagnosed on peripheral blood and bone marrow smears.

## Cytogenetics

Chromosome analysis showed the following karyotype:

46,XY,t(9;22)(q34;q11.2)[6]/46,idem,t(7;11)(p15;p15)[9].

### Treatment

Patient was treated initially with hydroxyurea, followed by Dasatinib but did not respond. High-dose ARA-C and subsequent bone marrow transplantation from a HLA haploidentical brother, were also unsuccessful.

### Prognosis

The prognosis in this single case of CML in blast crisis is unfavorable.

## Genes involved and proteins

### HOXA13 (homeobox A13)

#### Location 7p15.2

The HOXA13 gene is part of the HOXA cluster genes and contains 2 exons, encoding a protein of 338 amino acids with a homeodomain.

### NUP98 (nucleoporin 98 kDa)

#### Location 11p15.4

#### Protein

920 amino acids; 97 kDa; contains repeated motifs (GLFG and FG) in N-term and a RNA binding motif in C-term.

## Result of the chromosomal anomaly

### Fusion protein

#### Description

The NUP98/HOXA13 fusion protein consists of the N-terminal phenylalanine-glycine repeat motif of NUP98 and the C-terminal homeodomain of HOXA13, similar to the NUP98/HOXA9 fusion protein (Fujino et al., 2002; Romana et al, 2006).

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