

Leukaemia Section

Short Communication

t(11;12)(p15;q13) NUP98/HOXC11 t(11;12)(p15;q13) NUP98/HOXC13

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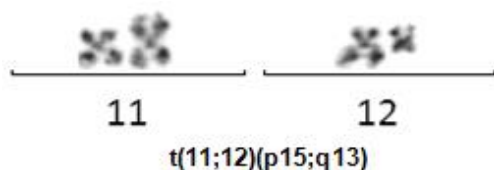
Abstract

Review on t(11;12)(p15;q13), with data on clinics, and the genes involved.

Keywords

Chromosome 11; Chromosome 12; NUP98; HOXC11; HOXC13; Acute myeloid leukemia; Therapy-related myeloid neoplasms

Identity



t(11;12)(p15;q13) G- banding - Courtesy Melanie Zenger and Claudia Haferlach.

Note

t(11;12)(p15;q13) with NUP98 and HOXC11 involvement has been described in 4 cases (Taketani et al., 2002; Gu et al., 2003), and with NUP98 and HOXC13 involvement in 3 additional cases (La Starza et al., 2003; Panagopoulos et al., 2003; Tomic et al., 2009)

Clinics and pathology

To be noted that NUP98 gene was found rearranged but HOXC genes were not tested or neither NUP98 nor HOXC genes were tested in 5 cases (Roulston et

al., 1998; and Kobzev et al., 2004 are identical cases), all of which were treatment-related MDS or AML (t-MDS or t-AML): a 9 mths old boy, 3 female patients aged 39 yrs, 41 yrs and 55 yrs, and one other male patient (Roulston et al., 1998; Nishiyama et al., 1999; Wong et al., 1998; Masuya et al., 2002; Kobzev et al., 2004; Schmidt-Hieber et al., 2010). Previous diseases were Hodgkin's disease in 2 cases, AML and breast cancer in one case each.

As noted by La Starza et al., 2009, a NUP98-positive acute myeloid leukemia with a t(11;12)(p15;q13) can occur without HOXC cluster gene involvement.

Disease

All the 7 cases with NUP98/HOXC hybrid gene were de novo acute myeloid leukemia: one AML without maturation (M1), four AML with maturation (M2), one acute myelomonocytic leukaemia (M4) and one acute monoblastic/monocytic leukaemia (M5b).

Epidemiology

Sex ratio was 2M/2F in HOXC11 cases and 0M/3F in HOXC13 cases; more cases are needed to determine if this discrepancy is coincidental/stochastic. Patients were aged 14, 22, 40 and 41 yrs in HOXC11 cases and 47, 57, 59 yrs in HOXC13 cases

Prognosis

Two cases were in complete remission (5 mths+, NA), and four cases were reported to have died (8 mths, 8mths, 19 mths, NA).

Cytogenetics

Cytogenetics morphological

The t(11;12)(p15;q13) was the sole abnormality in all the 7 cases with NUP98/HOXC hybrid gene ascertained. In the 5 cases of therapy-related leukemia without ascertainment of a NUP98/HOXC hybrid gene, the t(11;12)(p15;q13) was the sole abnormality in 2 cases, and additional abnormalities were found: a t(17;21)(q11;q22) with RUNX1 rearrangement in 1 case, a +21 in 1 case and a del(7q) and other abnormalities in 1 case.

Genes involved and proteins

NUP98 (nucleoporin 98 kDa)

Location

11p15.4

DNA/RNA

Alternate splicings

Protein

920 amino acids (aa) and other isoforms; NUP98 belongs to the nucleoporin gene family and encodes a 186 kDa precursor protein that undergoes autoproteolytic cleavage to produce a 98 kDa and 96 kDa nucleoporins. The 98 kDa nucleoporin contains a Gly-Leu-Phe-Gly (GLFG and FG) repeat in N-term, a GLEBS-like motif (which binds RAE1), and a RNA binding motif in C-term. NUP98 is involved in nuclear import/export, mitotic progression, and regulation of gene expression (Duheron and Fahrenkrog, 2015).

HOXC11

Location

12q13.13; Starts at 53973126 and ends at 53976419 bp from pter (according to hg38-Dec_2013)

DNA/RNA

915 nucleotids (nt), 2 exons

Protein

304 aa; the protein localizes in the nucleus; sequence-specific transcription factor which contains a homeodomain with helix-turn-helix (HTH) motif in aa 233 to 289. Part of the Hox clusters.

There is a timing mechanism to synchronize Hox gene expression during embryogenesis ("Hox clock").

HOX genes regulates the expression of genes that are implicated during embryogenesis (anterior-posterior patterning and limbs developments).

HOX genes are also expressed in adult tissues (review in Deschamps and Duboule, 2017).

HOXC13

Location

12q13.13; Starts at 53938792 and ends at 53946544 bp from pter (according to hg19-Feb_2009)

Note

HOXC13 starts 37627 nt after the end of HOXC11.

DNA/RNA

993 nt, 2 exons

Protein

330 aa; the protein localizes in the nucleus; sequence-specific transcription factor which contains a homeodomain with helix-turn-helix (HTH) motif in aa 260 to 319.

Part of the Hox clusters.

There is a timing mechanism to synchronize Hox gene expression during embryogenesis ("Hox clock").

HOX genes regulates the expression of genes that are implicated during embryogenesis (anterior-posterior patterning and limbs developments).

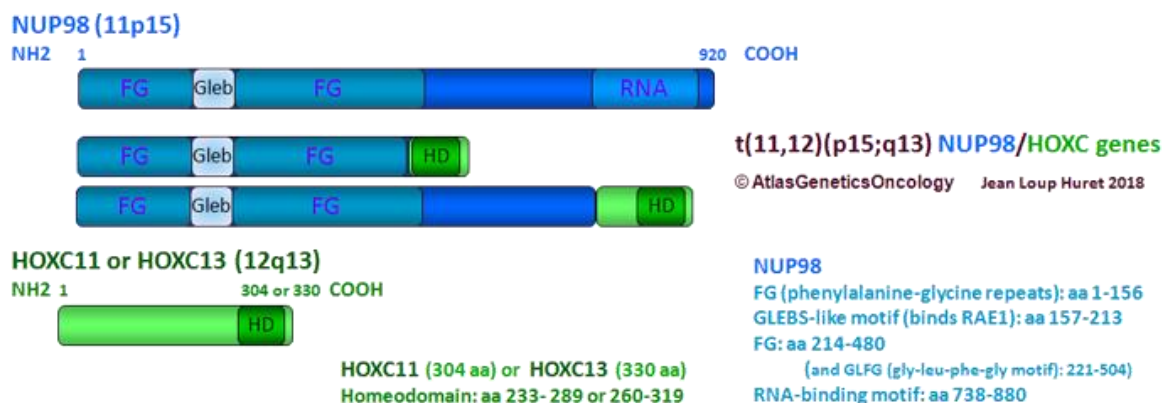
HOX genes are also expressed in adult tissues (review in Deschamps and Duboule, 2017).

Result of the chromosomal anomaly

Hybrid gene

Description

The NUP98 breakpoint was between exon 11 and 12 in three HOXC11 cases (Gu et al., 2003), and between exon 14 and 15 in the other HOXC11 case (Taketani et al., 2002). It was found between exon 15 and 16 in two HOXC13 cases (La Starza et al., 2003; Panagopoulos et al., 2003). The HOXC11 breakpoint was between exon 1 and 2 (Gu et al., 2003), or in exon 1 (Taketani et al., 2002). The HOXC13 breakpoint was between exon 1 and 2 (La Starza et al., 2003; Panagopoulos et al., 2003).



Fusion protein

Description

fuses the N-term NUP98 to the C-term of HOXC11 or HOXC13. This correspond to 469 aa or 628 aa from NUP98 in the HOXC11 cases and 715 aa in the HOXC13 cases fused to 77 aa from HOXC11 (Gu et al., 2003), or 120 aa from HOXC13 (Taketani et al., 2002).

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