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Leukaemia Section
Short Communication

t(10;17)(p15;q21) ZMYND11/MBTD1

Etienne De Braekeleer, Nathalie Douet-Guilbert, Audrey Basinko, Marie-Josée Le Bris, Frédéric Morel, Marc De Braekeleer

Cytogenetics Laboratory, Faculty of Medicine, University of Brest, France (EDB, NDG, AB, MJLB, FM, MDB)

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Abstract

Short communication on on t(10;17)(p15;q21) ZMYND11/MBTD1, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

Acute myeloid leukemia (AML), poorly differentiated, AML without maturation or with minimal maturation (AML-M0, and AML-M1)

Epidemiology

This is a rare chromosomal rearrangement, only reported in four cases of AML without or with minimal maturation, without molecular characterization (Pollak and Hagemeijer, 1987; Shah et al., 2001; Barjesteh van Waalwijk et al., 2003; Dicker et al., 2007).
We add two cases with molecular cytogenetic studies (Tempescul et al., 2007; De Braekeleer et al., 2014).There were 2 cases of AML-M0 and 4 cases of AML-M1.

Clinics

Patients were aged 11, 13, 16 and 40 years. There were 3 male and 3 female patients.

Treatment

Treatments of the patients reported in Tempescul et al. 2007, De Braekeleer et al. 2014 were the following: (P1) induction therapy followed by three consolidation courses leading to complete remission; (P2) induction therapy followed by consolidation therapy leading to complete remission, then relapse and second complete remission, then bone marrow transplantation.

Evolution

(P1) alive in complete remission 71 months following diagnosis; (P2) died 37 months following the initial diagnosis. Another patient reported in the literature was in complete remission at 42 months after diagnosis.

Cytogenetics

Note

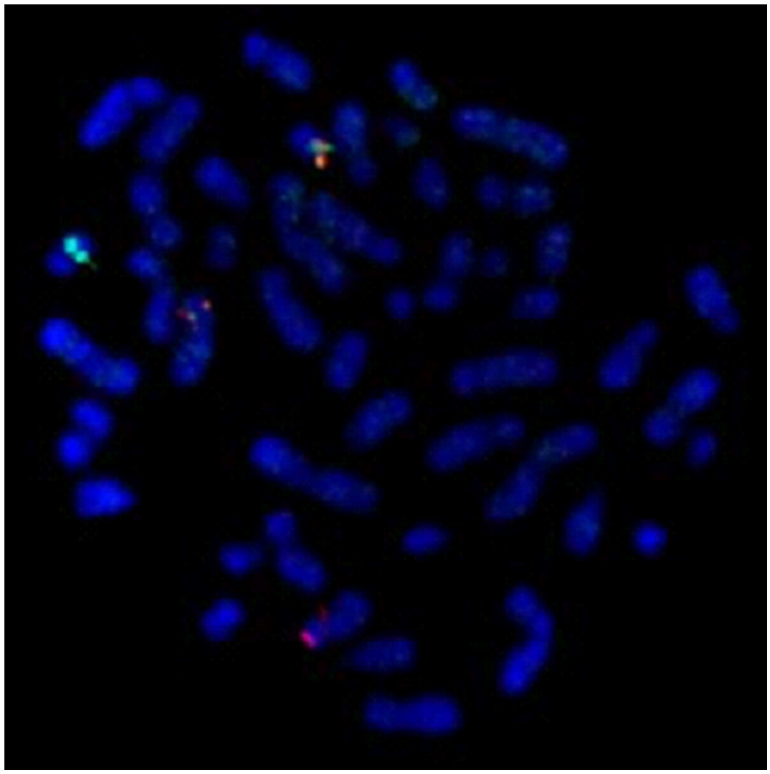
The t(10;17)(p15;q21) involves two genes that were not previously reported to form a putative fusion gene.

Cytogenetics morphological

t(10;17)(p15;q21) is identified by banding cytogenetics.

Cytogenetics molecular

To determine the position of the breakpoints on chromosomes 10 and 17, BACs located in the bands of interest were used as probes in FISH experiments. Analysis with RP11-387K19 showed that one signal hybridized to the normal chromosome 10, and the other split and hybridized to both der(10) and der(17). Analysis with RP11-326B24 showed that one signal hybridized to the normal chromosome 17, and the other split and hybridized to both der(17) and der(10). Co-hybridization with both BAC clones showed two fusion signals. RP11-387K19 contains the ZMYND11 gene and RP11-326B24 the MBTD1 gene.



FISH with BACs RP11-387K19 (spectrum orange, located in 10p15 and containing ZMYND11) and RP11-326B24 (spectrum green, located in 17q21 and containing MBTD1) showing co-hybridization.

Genes involved and proteins

ZMYND11

Location

10p15.3 (according to UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly)

DNA/RNA

The ZMYND11 gene contains 15 exons, of which 14 are coding, spanning 120 kb. Different isoforms are generated by seven alternatively spliced transcript variants (Hateboer et al., 1995).

Protein

The protein localizes to the nucleus and contains 3 motifs involved in transcription regulation: a PHD finger and bromodomain in its N-terminal half, and a MYND domain (conserved 2-zinc finger motif) at its C terminus. The MYND domain interacts with the N-CoR/mSin3/HDAC1 complex that causes transcriptional repression (Masselink and Bernards, 2000).

MBTD1

Location

17q21.33

DNA/RNA

The MBTD1 gene contains 17 exons, of which 15 are coding, spanning 82 kb. Seven transcript variants are known (Eryilmaz et al., 2009).

Protein

MBTD1 localizes to the nucleus and contains a FCS-type zinc finger at the N-terminus with putative regulatory function and four MBT (malignant brain tumor) repeats at the C-terminus. MBTD1 is a putative Polycomb group protein, which are known to maintain the transcriptionally repressive state of genes, probably via chromatin remodeling (Nady et al., 2012).

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