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# Leukaemia Section
## Short Communication

# t(20;21)(q13.2;q22.12) ZFP64/RUNX1

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

Cytogenetics Laboratory, Faculty of Medicine, University of Brest, France (NDG, ED, AB, MJL, FM, MD)

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## Clinics and pathology

### Disease

Chronic myelomonocytic leukemia (CMML)

### Epidemiology

This is a rare chromosomal rearrangement, only reported twice in myeloid hemopathies, without molecular characterization but for the case reported by Richkind et al. (2000) who showed rearrangement of RUNX1 (Secker-Walker et al., 1995; Richkind et al., 2000).

### Clinics

A 91-year old woman seen for fever and thrombopenia.

## Cytogenetics

**Note**

The t(20;21)(q13.2;q22.12) involves the RUNX1 (alias AML1) gene that acts as an activator or repressor of target gene expression depending upon the large number of transcription factors, coactivators and corepressors that interact with it. RUNX1 functions as an organizing protein that facilitates assembly of transcriptional activation or repression complexes.
All the translocations that retain Runt homology domain but remove the transcription activation domain have a leukemogenic effect by acting as dominant negative inhibitors of wild-type RUNX1 in transcription activation (De Braekeleer et al., 2011).

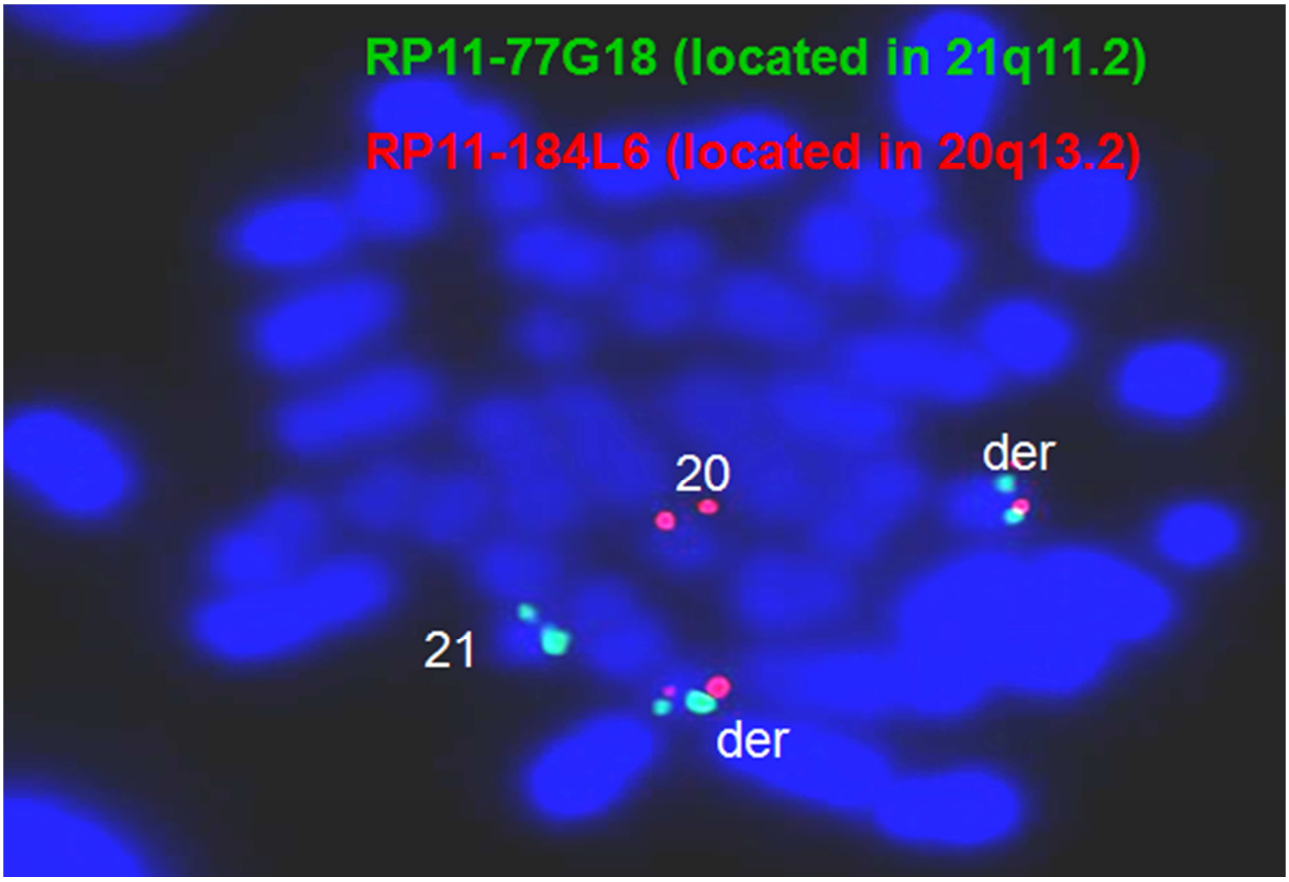
RHG banding showing chromosomes 20 and 21 and the derivatives der(20) and der(21).

### Cytogenetics morphological

t(20;21)(q13.2;q22.12) identified by FISH in a clone having a trisomy 8 (cryptic rearrangement).

### Cytogenetics molecular

FISH showed that the breakpoint on 21q22 was located in RUNX1. To confirm the position of the breakpoint on chromosome 20, BACs located at 20q13 were used as probes in FISH experiments. Analysis with RP11-184L6 showed that one signal hybridized to the normal chromosome 20, and the other splitted and hybridized to both der(20) and der(21). Co-hybridization with the RP11-184L6 clone and a RUNX1 probe (RP11-77G18) showed two fusion signals. RP11-184L6 contains the ZFP64 gene.




FISH with BACs RP11-77G18 (spectrum green, located in 21q22.12 and containing RUNX1) and RP11-184L6 (spectrum orange, located in 20q13.2 and containing ZFP64) showing co-hybridization of both derivative chromosomes.

## Genes involved and proteins

### *RUNX1*

**Location**
21q22.12

**Note**
RUNX1 belongs to a family of genes that share a 128 amino acid region of high sequence homology, known as the 'Runt domain', first identified in the Drosophila runt gene.
This 'Runt homology domain' is responsible for heterodimerization with the core-binding factor-b (CBF-b or PEBP2b) to form a transcription factor and for DNA binding.
RUNX1 acts as a key regulator of hematopoiesis through the regulation of various hematopoietic genes, including growth factors (GM-CSF, MPO and IL-3), surface receptors (TCRA, TCRB, M-CSF receptor and FLT3), signaling molecules (CDKN1A, BLK and BCL2) and transcription activators (STAT3 and MYB).

**DNA/RNA**
The RUNX1 gene spans 260 kb and consists of 12 exons with two distinct promoters.

At least 12 different RUNX1 mRNAs differing in their types of 5' and 3' untranslated regions (UTRs) and their coding regions are generated.

**Protein**
The RUNX1 protein contains a 'Runt homology domain' as well as transcription activation and inhibition domains.
It acts as an activator or repressor of target gene expression depending upon the large number of transcription factors, coactivators and corepressors that interact with it.
RUNX1 functions as an organizing protein that facilitates assembly of transcriptional activation or repression complexes.
By recruitment of non-DNA binding proteins as p300/CBP and histone acetyltransferase, it contributes to the activation of transcription of target genes.
Upon recruitment of non-DNA binding repressors such as mSin3A, Groucho/TLE and histone deacetylase, it represses transcription of target genes.

### *ZFP64*

**Location**
20q13.2

**DNA/RNA**

The ZFP64 gene contains 6 exons spanning 41 kb. Twelwe transcripts are known, of which 9 are protein coding.

**Protein**

ZFP64 protein belongs to the krueppel C2H2-type zinc-finger protein family and contains 9 C2H2-type zinc fingers.

It may be involved in transcriptional regulation. It interacts with the intracellular domain of Notch1, and acts as a coactivator of the Notch intracellular domain (Sakamoto et al., 2008).

# References

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