

# A novel t(2;10)(q31;p12) balanced translocation in acute myeloid leukemia

Luciana Impera,<sup>1</sup> Giulia Daniele,<sup>1</sup>  
Luisa Marra,<sup>1</sup> Carmen Baldazzi,<sup>2</sup>  
Ilaria Iacobucci,<sup>2</sup> Giovanni Martinelli,<sup>2</sup>  
Nicoletta Testoni,<sup>2</sup>  
Clelia Tiziana Storlazzi<sup>1</sup>

<sup>1</sup>Department of Biology, University of Bari; <sup>2</sup>Institute of Hematology and Medical Oncology Lorenzo e Ariosto Seràgnoli, Sant'Orsola-Malpighi Hospital, University of Bologna, Italy

## Abstract

We describe a case of acute myeloid leukemia M5 showing a balanced t(2;10)(q31;p12) translocation. This has never been described before as the sole cytogenetic abnormality in a bone marrow cell clone at onset. Using fluorescence *in situ* hybridization with properly designed bacterial artificial chromosome probes, we mapped the breakpoint regions on both derivative chromosomes 2 and 10: der(2) and der(10), respectively. The *MPP7* gene, disrupted by the breakpoint on chromosome 10, was juxtaposed upstream of both *HNRNA3* and *NFE2L2* genes on chromosome 2, without the formation of any fusion gene. Using real-time quantitative polymerase chain reaction, we tested the possible dysregulation of any of the breakpoint-associated genes as a consequence of the translocation, but we found no statistically significant alteration. Considering the potential role of this clonal cytogenetic abnormality in leukemogenesis, we speculate that this translocation could have an impact on additional genes mapping outside the breakpoint regions. However, the limited amount of RNA material available prevented us from testing this hypothesis in this present case.

## Introduction

The majority of chromosomal rearrangements in acute myeloid leukemia (AML) result in fusion genes or position effects. Indeed, according to the World Health Organization classification of hematopoietic tumors,<sup>1</sup> a consistent group of aberrations is associated with specific AML subtypes, with both diagnostic and prognostic significance.

In this report, we describe a case of AML (FAB M5 subtype) in which the karyotype displayed a novel t(2;10)(q31;p12) balanced

translocation as the sole cytogenetic abnormality in a bone marrow cell clone at onset.

## Case Report

In November 2007, a 42-year old man was admitted to the Department of Hematology and Oncological Sciences of the Seràgnoli Institute, Bologna, northern Italy. He presented with a fever and leukocytosis. Peripheral blood count showed white blood cells  $81.7 \times 10^9/L$  with 9% neutrophils and 84% blast cells, hemoglobin 12 g/dL, and platelets  $89 \times 10^9/L$ . Bone marrow aspirate was hypercellular and showed a wide population of medium and large sized cells characterized by a high nuclear/cytoplasmic ratio and basophil cytoplasm. Immunophenotyping identified a CD13<sup>+</sup>, CD15<sup>+</sup>, CD33<sup>+</sup>, CD117<sup>+</sup>, MPO7<sup>+</sup> population with aberrant expression of CD19. Bone marrow biopsy confirmed a widespread infiltrate with CD68 (PGM1) positive blast cells. A diagnosis of acute monoblastic leukemia was made. Cytogenetic analysis showed the karyotype 47,XY,+8[5]/46,XY,t(2;10)(q33;p12)[4]/46,XY[21]. Mutational analysis was negative for FLT3-ITD, FLT3-TKD and NPM1. In December 2007, induction chemotherapy with fludarabine (50 mg/die for 5 days), cytosine arabinoside (Ara-C) (4 g/die for 5 days), idarubicin (20 mg/die on Days 1, 3 and 5) followed by gemtuzumab-ozogamicin infusion (5 mg on Day 6) was started and a morphological and cytogenetic remission was achieved. The patient later received a first consolidation cycle with idarubicin and Ara-C, and a second consolidation cycle with high-dose Ara-C. In May 2008, bone marrow examination revealed an initial relapse, confirmed by the cytogenetic analysis showing karyotype 47,XY,+8[8]/46,XY[22]. Reinduction chemotherapy was started but the patient showed resistance to conventional chemotherapy. In June 2008, he started therapy with tipifarnib and bortezomib, but he experienced disease progression with peripheral blastosis, anemia and thrombocytopenia. He died 11 months after diagnosis from infectious complications.

Fluorescence *in situ* hybridization analysis mapped the chromosome 2 breakpoint within RP11-25L17 (chr2:177,938,840-178,096,310), precisely within the non-overlapping region (approx. 70 Kb) of this clone with RP11-28M17 (chr2:178,009,023-178,198,838) (Figure 1A). The breakpoint was then located upstream from the *heterogeneous nuclear ribonucleoprotein A3* (*HNRNPA3*) gene, encoding a protein involved in alternative splicing,<sup>2</sup> and the *nuclear factor erythroid 2-like 2* (*NFE2L2*) gene, encoding a basic leucine zipper (bZIP) transcription factor.<sup>3</sup> Interestingly, both genes had been previously described as deregulated

Correspondence: Clelia Tiziana Storlazzi, Department of Biology, University of Bari, via G. Amendola 165/A, 70126 Bari, Italy. Tel. +39.080.5443582 - Fax: +39.080.5443386. E-mail: cleliatiziana.storlazzi@uniba.it

Key words: chromosome, translocation, FISH, acute myeloid leukemia, *HNRNA3*, *NFE2L2*, *MPP7*.

Acknowledgments: this work was supported by the Italian Cancer Research Association (Associazione Italiana per la Ricerca sul Cancro, AIRC) and the Ministry of Education and Research (Ministero dell'Istruzione, dell'Università e della Ricerca, MIUR).

Received for publication: 13 November 2012.  
Accepted for publication: 30 November 2012.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright L. Impera et al., 2012  
Licensee PAGEPress, Italy  
Hematology Reports 2012; 4:e27  
doi:10.4081/hr.2012.e27

in some tumor types.<sup>4,5</sup> On chromosome 10, the breakpoint was identified by the splitting signals of RP11-49D12 (chr10:28,369,837-28,539,930) on both der(2) and der(10) (Figure 1A). It encompassed the *palmitoylated membrane protein 7* (*MPP7*) gene, encoding a member of the p55 subfamily of MAGUK proteins.<sup>6</sup>

Neither of these two breakpoint regions has ever been described as being involved in tumor-associated chromosome rearrangements.

To assess the possible impact of this translocation on the *HNRNPA3*, *NFE2L2*, and *MPP7* genes, real-time quantitative polymerase chain reaction assays were performed on the patient's bone marrow (BM) RNA, and compared to 4 AML M5 control cases (without the translocation), as well as to normal BM. We used three reference genes (*HPRT1*, *YWHAZ*, and *SDHA*) and the mean expression value of the control AMLs as calibrator. The results obtained showed that there was no statistically significant change in the expression of any of the genes investigated (Figure 1B).

## Discussion and Conclusions

To summarize, we describe for the first time a novel, non-recurrent t(2;10)(q31;p12) translocation in AML which did not lead to any gene fusion or position effects. Remarkably, the molecular consequences of this translocation are to be found outside the breakpoint regions' gene domains. We might speculate

