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

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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 disregulation 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.

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 in some tumor types. On chromosome 10, the breakpoint was identified by the splitting signals of RP11-49D12 (chr10:28,369,837-28,539,330) 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. 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 HNRNA3, 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 a calibrator. The results obtained showed that there was no statistically significant change in the expression of any of the genes investigated (Figure 1B).
that the chromatin relocation due to the t(2;10)(q31;p12) rearrangement might have influenced the expression pattern of additional genes, mapping along both derivative chromosomes 2 and 10. However, we were not able to evaluate this because of the limited amount of RNA material available.

It is not possible to draw clear conclusions about the possible clinical impact of this translocation, also because the rearrangement was not present at relapse. However, on the other hand, the t(2;10)(q31;p12) was the only chromosomal aberration observed in the karyotype of a cell clone in the patient’s bone marrow at onset, suggesting it might have an impact on leukemogenesis. Notably, the patient was negative for FLT3 and NPM1 mutations, excluding the possibility that this translocation might be a secondary event to this type of alteration. The study of further AML cases with t(2;10)(q31;p12) would allow us to gain a better understanding of the clinical and molecular impact of this translocation on patient outcome.

References
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Figure 1. A) Left: Fluorescence in situ hybridization (FISH) results obtained with bacterial artificial chromosome clones delimiting the breakpoint regions on der(2) and der(10). Right: Maps of the breakpoint regions in chromosome bands 2q31.2 (top) and 10p11.23 (bottom), according to the latest release of the UCSC Human Genome Browser (GRCh37/hg19) (February 2009). Genes are indicated by yellow bars. The reported clones have the same color code as the FISH image on the left. B) Expression analyses of exons 6 and 14 of MPP7 (red bars), exon 5 of HNRNPA3 (green bar), and exon 4 of NFEL2L2 (yellow bar) evaluated by real-time quantitative polymerase chain reaction, in the present case [t(2;10)], 4 control acute myeloid leukemia (AML) M5 samples, the mean Ct value of the controls (mean value), and normal bone marrow. The results showed comparable genes transcriptional levels in the patient with t(2;10) compared with the mean Ct value of the 4 M5 AML controls.