

Identification of PML/RAR α fusion gene transcripts that showed no t(15;17) with conventional karyotyping and fluorescent in situ hybridization

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ABSTRACT. Acute promyelocytic leukemia (APL) is characterized by a reciprocal translocation, t(15;17)(q22;q11-21), resulting in the fusion of the promyelocytic leukemia (*PML*) and retinoic acid receptor alpha (*RAR α*) genes. Using conventional cytogenetic methods, these translocations are normally detected in about 70-90% of patients; most negative results are due to technical problems or cryptic variants. These masked *PML/RAR α* fusions can be identified by molecular analyses, such as reverse transcriptase-polymerase chain reaction (RT-PCR) or fluorescence *in situ* hybridization (FISH). Approximately 5 to 10% of all APL cases reported do not show *PML/RAR α* fusion transcripts, even with dual-colored FISH. We report three of 40 diagnosed APL cases that showed morphological, cytochemical, and immunophenotypic features of hypergranular APL, but did not show a *PML/RAR α* fusion signal or any of its variants, on FISH. All cases were identified by RT-PCR, which

was further confirmed by cDNA sequencing. Conventional karyotyping showed other clonal aberrations in these cases, but failed to show t(15;17) or any other variants or complex translocations.

Key words: Acute promyelocytic leukemia; Cryptic insertions; Promyelocytic leukemia/retinoic acid receptor alpha; Reverse transcription-polymerase chain reaction; Fluorescence *in situ* hybridization; Sequencing analysis