Hematology-2013
OMICS Group Conferences
Accelerating Scientific Discovery
International Conference on
Hematology & Blood Disorders
September 23-25, 2013 Raleigh, USA

# Identification of novel molecular markers for minimal residual disease assessment in acute leukemia

**Sona Pekova**
*CHAMBON, Czech Republic*

**Abstract**

Acute leukemias (AL) are a heterogeneous group of hemato-oncologic disorders, generally involving two types of AL – acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). They have varying prognoses that are reliant on timely and correct diagnosis. Because of the great biological diversity in AL, it is difficult to predict an individual patient‘s response to treatment. At diagnosis, approximately 50 % of AML cases and 70 % of ALL cases harbor clonal chromosomal abnormalities. Some of these chromosomal changes result in the formation of a fusion product, which can be sensitively detected and quantified using molecular techniques, thus superseding standard cytogenetic or flow-cytometric analyses. Fusion transcripts that can be monitored at the RNA level include AML1-ETO (RUNX1-RUNX1T1), PML-RARα, DEK-CAN (DEK-NUP214), and CBFβ-MYH11 in AML, and BCR-ABL, MLL-AF4 (MLL-AFF1), E2A-PBX1 (TCF3-PBX1), TEL-AML1 (ETV6-RUNX1) in ALL. In addition to fusion transcripts, mutations of clinically relevant genes such as NPM1, CEBPα, FLT3, c-KIT, WT1 can also be identified by molecular methods. In ALL, immunoglobulin heavy chain (IGH) and T-cell receptor (TCR) gene rearrangements are frequent targets.

All of these chromosomal aberrations, gene mutations and gene rearrangements can be used to sensitively and quantitatively detect residual leukemic cell populations, and thus used to 2 monitor minimal residual disease (MRD). In recent years, several studies of childhood and adult AL cases have demonstrated MRD to be an important independent predictor of high clinical relevance. Measurement of MRD allows assessments of the quality of treatment response, duration of complete remission and prediction of the individual risk of relapse. Currently, molecular technologies based on real-time PCR have been established as being sensitive and specific, and have become the gold standard for diagnosing AL and evaluating MRD. However, these methods are not suitable for patients in whom none of the routinely analyzed aberrations have been identified. It is therefore highly desirable to identify new clone-specific markers of leukemic cells to follow up MRD in such patients.

The aim or our study was to develop a technique allowing us to identify new unique clone-specific markers at the cytogenetic level and characterize them down to the molecular level (specific nucleotide sequence). Briefly, chromosomal aberrations were identified using molecular cytogenetic techniques (mFISH, mBAND), these aberrations were then microdissected using fine needle micromanipulator, the resulting DNA fragments were whole-genome amplified, and using next-generation sequencing precise mapping of the novel chromosomal breakpoints at the nucleotide level was performed (Figure 1). This combined approach allowed us to design real-time MRD PCR assays based on unique genetic markers of AL blasts in order to specifically and sensitively monitor the dynamics of the malignant clone in response to patient treatment.