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Identification of new molecular markers for minimal residual disease assessment in acute leukemia patients

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Acute leukemia (AL) comprises a heterogeneous group of hematologic malignancies with varying prognoses. In light of this heterogeneity, individual patient response to treatment can be difficult to predict. Sensitive monitoring of residual leukemic cell populations (minimal residual disease - MRD) is thus very important and holds great potential for improving treatment strategies. Commonly used MRD targets include recurrent cytogenetic abnormalities and mutations in important hematological genes; unfortunately such targets are identified in majority of adult ALL patients and in only about 50 % of adult AML patients. Identification of new specific molecular markers of leukemic blasts for MRD assessment is therefore highly desirable.

Our goal was to develop a unique technical approach for the identification and mapping of clone-specific chromosomal abnormalities down to the single nucleotide level using current molecular cytogenetic techniques, particularly multicolor fluorescence *in situ* hybridization, multicolor chromosome banding (mFISH, mBAND) and multiplex hybridization of fluorescently labeled BAC clones (BAC-FISH). Higher resolution was achieved by hybridization of fluorescent probes to combed DNA fibers (molecular combing, fiber-FISH). Another approach used for the precise identification of chromosomal breakpoints was chromosome microdissection followed by next-generation sequencing (NGS) of the dissected material. Finally, a specific Real-Time PCR assay to monitor MRD was designed.

Modern technologies open new vistas in the detection and identification of unique clone-specific abnormalities in AL patients. Our work clearly suggests that walking from the chromosomal level to the nucleotide level is feasible and readily applicable for eligible AL patients, allowing its use in standard clinical practice and as a tool for personalized „tailor-made“ medicine.

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