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Diagnostic biochips for the analysis of tumor biomarkers

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Genetic aberrations in leukemia often lead to the formation of expressed chimeric genes, which should be assessed for proper diagnosis and therapy. We developed a biochip-based assay for the analysis of 22 most clinically relevant fusion genes occurring in pediatric leukemia, including 8 recurrent translocations involved the MLL gene and different gene partners. The method includes a multiplex reverse transcriptase–polymerase chain reaction (RT–PCR) to amplify and fluorescently label a fusion transcript fragments and subsequent hybridization of on a biochip with immobilized oligonucleotides complementary to different parts of fusion genes. The fine structure of the MLL fusion genes, including localization of the MLL breakpoints, was performed in 43 infants and 28 pediatric cases. Other important cancer biomarkers predicting prognosis and therapeutic targets are somatic mutations in solid tumors. A diagnostic biochip for the detection of 39 clinically relevant somatic mutations in the BRAF, NRAS, KIT, GNAQ, GNA11, MAP2K1 and MAP2K2 genes has been developed. The multiplex LNA-clamp PCR was used for the preferable amplification of mutated over wild type DNA. The approach could detect 0.5% of mutated DNA in the sample analyzed.

The biochip-based assay is a robust and highly sensitive method for the detection of fusion genes and somatic mutations in cancer patients.

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