

Comprehensive liquid biopsy analysis as a tool for the early detection of minimal residual disease in breast cancer

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Liquid biopsy (LB) provides a unique minimally invasive tool to follow-up cancer patients over time, to detect minimal residual disease (MRD), to study metastasis-biology and mechanisms of therapy-resistance. Molecular characterization of CTCs offers additionally the potential to understand resistance to therapy and implement individualized targeted treatments which can be modified during the disease evolution and follow-up period of a patient. In this study, we present a long-term follow-up of operable breast cancer patients based on a comprehensive liquid biopsy analysis. A comprehensive liquid biopsy analysis was performed in peripheral blood of 13 patients with early-stage operable breast cancer at several time points for a period of ten years, consisting of: (a) CTC enumeration using the CellSearch system, (b) phenotypic analysis of CTCs using Immunofluorescence, (c) gene expression analysis, in EpCAM⁽⁺⁾ CTCs for CK-19, CD24, CD44, ALDH1, and TWIST1, (d) analysis of PIK3CA and ESR1 mutations in EpCAM⁽⁺⁾ CTCs and corresponding plasma ctDNA and (e) DNA methylation of ESR1 in CTCs. The molecular characteristics of CTCs were highly different even for the same patient at different time points, and always increased before the clinical relapse. Our results indicate that liquid biopsy can reveal the presence of MRD at least 4 years before the appearance of clinically detectable metastatic disease demonstrating that a comprehensive liquid biopsy analysis provides highly important information for the therapeutic management of breast cancer patients.