Molecular analysis and clinical value of circulating tumor cells (CTCs) identified via CytoTrack system in metastatic breast cancer patients.

Abstract

Background:
Luminal breast cancer is the most common subtype of breast cancer and has the best prognosis. However, approximately 40% of patients with this subtype can develop distant metastases, dramatically worsening the patient's survival. Monitoring metastatic Breast Cancer (MBC) for signs of progression is an important part of disease management. Circulating tumor cells (CTCs) detection and molecular characteristics gain importance as a diagnostic tool, but do not represent a clinical standard and its value as a predictor of progression is not yet established. This work aims to establish clinical value of the CTCs and their molecular characteristics.

Methods:
CTCs were detected and isolated using novel image-based and EpCAM-independent system CytoTrack. In total, 237 patients with diagnosed luminal MBC were enrolled in the study between June 2018 and October 2020. The PBMCs isolated from whole blood samples were stained and further analyzed via CytoTrack system. Identified CTCs were visualized and gained images were used for EpCAM expression analysis. Next, the single CTCs were isolated via micromanipulation and subjected to whole genome amplification, followed by genetic analysis with next generation sequencing (NGS).

Results and Conclusions:

The prognostic value of high CTCs count (≥5 CTCs) was maintained during the observation period. Moreover, the rising counts of CTCs during treatment were also identified as the unfavorable risk factor. Furthermore, the constant low CTCs count (<5 CTCs) during treatment was identified as strong favorable factor for prognosis in metastatic breast cancer patients. These findings are highly relevant for improving prognostication in metastatic breast cancer and in helping clinicians monitor patients during systemic therapy. Moreover, in our study we described the difference in EpCAM expression between CTCs clusters and single CTCs. The high heterogeneity of CTCs in EpCAM status, highlights the phenotypic plasticity of single cells. Additionally, this work also confirmed the great genomic heterogeneity of circulating tumor cells. The result of this study highlights the clinical utility of the CTCs detection and enumeration during the treatment in metastatic breast cancer patients.