Background

Despite initially successful therapeutic management of breast cancer, a relevant percentage of patients relapse with metastatic disease. The genetic understanding underlying this aspect is still fragmentary but circulating tumor cells (CTCs) represent today a reliable and non-invasive disease monitoring strategy, and offer repeatable access to the detection of tumor genetic heterogeneity. In this study we performed genetic characterization on pure single CTCs isolated from metastatic breast cancer patients, aiming to provide a full genetic picture of multiple single CTCs for each patient.

Methods

Peripheral blood from 4 de novo diagnosed metastatic breast cancer patients, ER+/HER2−, treated either with hormonal or chemotherapy as first line therapy, was collected at three different time points (before start, after one cycle of treatment and at tumor progression). The CTC enrichment and staining was performed with the CellSearch® system and from each sample individual CTCs were sorted with DEPArray™ platform. The DNA of each single CTC was amplified with Ampli™ WGA kit and Genome Integrity Index (GI) was assessed by Ampli™ QC kit. WGA output was used for genome-wide single cell copy number variation (CNV) analysis with Agilent SurePrint 1M array for comparative genomic hybridization (aCGH). Furthermore Ampli™ WGA products were also sequenced with Ampli™ CHP Custom Panel Beta on the Ion Torrent PGM 1400x average coverage on Ion 316 or 318 chip.

Conclusions

Breast Cancer CTCs display different types and degrees of heterogeneity in genomic aberrations both at the level of CNVs and Sequence variants. The preliminary results from this longitudinal study show clear evidence of dynamic changes in the genome as well the possibility for stable genomic CNV profile across time points and between cells. Although we characterized only 32/69 (46%) of isolated CTCs with high GI, the data we obtained supports the existence of a variable degree of heterogeneity. Characterizing all available cells may give more representative, deeper evaluation. Further investigation is warranted to correlate the impact of this heterogeneity and dynamics in relation to treatment selection and patient clinical management.