Identification of atypical cells in the blood of non-small cell lung cancer (NSCLC) patients

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Background & objectives

Background: Identifying the presence of circulating tumor cells (CTCs) is essential with regards to their metastatic potential, especially in lung cancer patients where 40% of them are diagnosed with metastatic disease. CTC detection in lung cancer patients with conventional epithelial biomarkers (Pan-cytokeratin (CK), Epithelial cell adhesion molecule (EpCAM)) is still challenging owing to clonal heterogeneity. Complete or partial loss of epithelial phenotype in response to epithelial to mesenchymal transition (EMT) could explain the limited frequency of CTCs in the blood of lung cancer patients. Recently, other cellular components including cancer-associated macrophage-like cells (CAMLs) were described at late-stage carcinoma including NSCLC patients.

Objective: Genomic profiling of potential CAML cells and any atypical cells found in the blood of NSCLC patients.

Methods

Methods: CTC detection in 68 advanced stage NSCLC patients (stage IIIA-IV) was performed using the microfluidic based CTC enrichment system (Parsortix^{TM}). Classical CTCs were identified upon immunofluorescence (IF) of cells with round shape, $CD45^-$, CK^+ and a clear nuclei signal. CAML were defined as enlarged phagocytic macrophage-like cells ranging from 30 to 300 µm in length. Micromanipulation of a subset of cells of interest allowed single cell isolation for consequent whole genome amplification (WGA) for low-pass genome sequencing with the Illumina platform and copy number alterations (CNAs) calling from single cells.

Results

Results: CTC slides from 68 patients were manually screened and classical CTCs were detected in 39.7% of the patients. Furthermore, in 26.5% of patients, aberrant $CK^-/CD45^-$ cell clusters were observed. CAMLs cells were detected in 29.4% of the patients. Interim survival analysis did not reveal any clinical association so far. Of the 21 cells with successful WGA, 15 (5 CAML, 4 potential CK^- clusters, 4 classical CTCs and 2 leukocytes as controls) underwent low-pass genome sequencing for CNA calls. Aberrant CNA profiles were observed in 1/5 CAML, 3/4 classical CTCs and 2/4 CK^- cell cluster.

Conclusion

Conclusion: We report the presence of aberrant $CK^-/CD45^-$ cell clusters and aberrant CAML in the blood of NSCLC patients. A great heterogeneity in atypical cells can be seen in the blood of NSCLC patients with some of these cells being of malignant origin.